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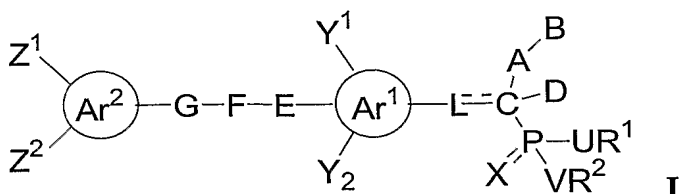
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(54) Title: HETEROARYL PHOSPHINYL AND THIOPHOSPHINYL COMPOUNDS FOR REGULATION OF GLUCOSE, TRIGLYCERIDES, AND LDL/HDL LEVELS



(57) Abstract: The invention provides phos-  
phorus-containing compounds, pharmaceutical  
formulations comprising the compounds, and  
methods of administering the compounds to a subject,  
wherein the compounds are of the Formula I wherein  
A, B, D, L, Ar<sup>1</sup>, Ar<sup>2</sup>, Y<sup>1</sup>, Y<sup>2</sup>, Z<sup>1</sup>, Z<sup>2</sup>, E, F, G, X, U, V,  
R<sup>1</sup>, and R<sup>2</sup> are as defined herein.

## HETEROARYL PHOSPHINYL AND THIOPHOSPHINYL COMPOUNDS FOR REGULATION OF GLUCOSE, TRIGLYCERIDES, AND LDL/HDL LEVELS

### FIELD OF THE INVENTION

5           The present invention relates to phosphorus-containing compounds, pharmaceutical formulations comprising phosphorus-containing compounds, and uses thereof. More specifically, the present invention relates to aryl and heteroaryl phosphonates, processes for their preparation, pharmaceutical formulations comprising them, and their use in methods of regulating plasma levels of glucose, triglycerides,  
10   and/or HDL/LDL.

### BACKGROUND OF THE INVENTION

Compounds that can bind as ligands for a variety of nuclear hormone receptors, particularly to a sub-family of nuclear hormone receptors that are activated by ligand binding and heterodimerization with retinoid X receptor (RXR) nuclear hormone  
15   receptors can be effective in regulating metabolic processes. Such receptors include peroxisome proliferator activated receptor (PPAR $\alpha$ , PPAR $\beta$ , PPAR $\gamma$ ), farnesoid X receptor (FXR), liver X receptor (LXR $\alpha$ , LXR $\beta$ ), vitamin D receptor (VDR), thyroid hormone receptor (TR), and retinoic acid receptor (RAR). These receptors are important regulators of metabolism, and are involved in multiple signal transduction pathways.  
20   Therefore compounds that modulate these receptors can be useful drugs for treatment of a wide range of metabolic disorders, including, for example, hypercholesteremia, hypertriglyceridemia, low HDL-C atherosclerosis, hyperglycemia, syndrome X, hyperinsulinemia, and diabetes.

Aralkyl phosphonates have been disclosed with biological activity in a variety of  
25   metabolic disease states. For example, some phosphonates reduce total plasma concentrations of cholesterol in many species, [Phan, et al., WO 02/26752]. This effect is

caused by major reductions in the plasma Low Density Lipoprotein (LDL-C) fraction. High total cholesterol levels have been shown to correlate with increased morbidity and mortality in epidemiological studies [Framingham Heart Study, Canadian Journal of Cardiology 4 suppA, 5A-10A (1988)]. In this and many similar studies the increased risk  
5 was associated with the LDL-C levels, and high HDL-C levels were associated with a decreased risk of CV disease and mortality. Reductions in total cholesterol, especially through treatment with HMG CoA reductase inhibitory "statins" which lead to dramatic reductions in LDL, have been shown to be beneficial in both preventing cardiovascular disease and in decreasing overall mortality. These same phosphonate compounds have  
10 been disclosed as useful for regulating the amount of Lp(a), a LDL-like lipoprotein wherein the major lipoprotein, apo B-100, is covalently linked to an unusual glycoprotein, apoprotein(a), in blood. [Phan, et al., WO 02/26752]. The covalent association between apo(a) and apo B to form Lp(a) is a secondary event which is independent of the plasma concentration of apo B. Due to its structural similarity to plasminogen, apo(a) interferes  
15 with the normal physiological thrombosis-hemostasis process by preventing thrombolysis, that is clot dissolution. The structural feature of Lp(a), where the LDL lipoprotein is linked to apo(a), is thought to be responsible for its atherogenic and thrombogenic activities.

Furthermore, aralkyl phosphonates have been disclosed which raise the amount of  
20 the High Density Lipoprotein in serum, [Phan et al. WO 03/070169]. Increases in HDL are strongly correlated with decreased cardiovascular disease risk in man, although to date only niacin has been shown to raise HDL in humans by 20% or more. In the HDL intervention trial [Rubins et al., New England Journal of Medicine 34, 410-418, (1999)], even a 6% increase in plasma HDL was shown to correlate with over a 20% decrease in  
25 cardiac morbidity and mortality.

The cardioprotective effects of HDL-C are believed to be derived from two major processes. One is the known antioxidant effects of certain HDL subfractions, and the other is the role of HDL in Reverse Cholesterol Transport (RCT), the process by which cholesterol is removed from peripheral tissues, and returned to the liver. In

5 atherosclerosis, it is believed that the disease process involves macrophages which are involved in removing cholesterol-rich lipid deposits from the arterial intima. Normally, these macrophages ingest lipid residues on the surface of the intima, and then secrete cholesterol which is incorporated into HDL particles, where they are turned into cholesteryl esters, and then absorbed into the liver through SR-B1 scavenger receptors.

10 Once in the liver, a major route of cholesterol disposal is conversion into bile acids and secretion in bile. In atherosclerotic lesions, this process appears to become highly disregulated, and the macrophages absorb large amounts of lipid, but do not successfully package it into HDL, with the result that they fill up with cholesterol-rich lipids and become foam cells, a major component of the atherosclerotic plaque.

15 The aralkyl phosphonates described in Phan et al. WO 03/070169 and WO 03/070179 also cause macrophages to secrete large quantities of Apo E. This apolipoprotein is a minor component of HDL, and may well be involved in RCT from macrophages and the arterial intima. In ApoE <sup>-/-</sup> mice atherosclerotic disease occurs very quickly, and the disease progression can be halted by transfecting Apo E back into the

20 mice, suggesting that Apo E is cardioprotective. Furthermore, Apo E has been shown to have strong antioxidant properties, and may be useful in neuroprotective indications.

As mentioned above, cholesterol is secreted from the liver as bile acids, which are derived from cholesterol by a series of oxidative steps. When bile acids are secreted from the liver, they also contain cholesterol itself, which can either be excreted or reabsorbed

25 lower in the GI tract. Bile acids turn out to be ligands for the FXR receptor, one of the

RXR heterodimerizing nuclear hormone receptors. FXR controls a lot of genes involved in cholesterol homeostasis, and the bile acid/FXR interaction is undoubtedly one of the most important feedback loops in cholesterol homeostasis.

Many tissues either do not rely on HDL at all, or only in part for RCT. The other  
5 major pathway of cholesterol secretion from tissues is side chain hydroxylation of cholesterol, to give the so-called oxysterols. These compounds have considerably more water solubility than cholesterol itself, and have carrier proteins in plasma. Once excreted into plasma, they are also absorbed by the liver, and then further processed, some into bile acids. The LXR heterodimeric nuclear hormone receptor is an oxysterol  
10 receptor, and controls many genes involved in cholesterol homeostasis, similar to FXR.

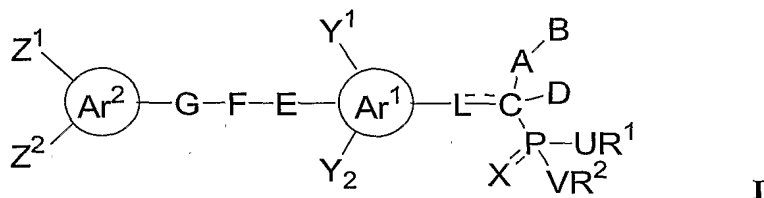
The PPAR family of RXR-heterodimerizing nuclear hormone receptors is very important in metabolic regulation. PPAR $\alpha$  is the target of the fibrate drugs, which can raise HDL, and marginally lower LDL, and also strongly reduce triglycerides. PPAR $\alpha$  agonists have also been revealed to have anti-obesity effects, presumably due to their  
15 effects on lipid metabolism [Willson, US Patent 6,028,109]. PPAR $\gamma$  agonists, such as Rosiglitazone and Pioglitazone are marketed for lowering blood glucose in diabetics. These compounds can also show effects on serum cholesterol and triglycerides, both of which were lowered by Troglitazone, but raised by Rosiglitazone. Although PPAR $\beta$  is less well characterized than the other PPARs, it also appears to be strongly involved in  
20 metabolic regulation and there are claims that using PPAR $\beta$  agonists leads to lower total cholesterol levels [Shimokawa et al., US Patent 6,300,364].

Retinoids, such as Accutane, also have effects on metabolism, with raised triglyceride levels being a major side effect of Accutane treatment.

All of this data taken together suggests that the RXR-heterodimerizing nuclear hormone receptors are involved in a very complicated cross-regulation of metabolism, energy utilization and cholesterol homeostasis. Therefore ligands which modulate this system in favourable ways should be useful in the treatment of metabolic diseases such as dyslipidemias and diabetes. The compounds of the current invention are phosphorus-based ligands for several of these receptors, and therefore are useful in treating metabolic disease conditions, and the diseases which arise from metabolic imbalances such as atherosclerosis.

### SUMMARY OF THE INVENTION

The present invention provides aryl and heteroaryl phosphorus-containing compounds, or pharmaceutically acceptable salts thereof, of the Formula (I):



wherein

A is a bond, O, CH<sub>2</sub>, CHF, CF<sub>2</sub>, or NR<sub>6</sub>;

B is H, C<sub>1</sub>-C<sub>6</sub> lower alkyl, or P(=X<sup>1</sup>)(UR<sup>3</sup>)(VR<sup>4</sup>);

D is a) H or lower alkyl, wherein the L=C bond is a single bond; or

b) OH, OCOR<sup>5</sup>, NH<sub>2</sub>, NR<sup>6</sup>R<sup>6a</sup>, or NHCOR<sup>5</sup>, wherein the L=C bond is a single bond, with the proviso that A is CH<sub>2</sub>, CHF, CF<sub>2</sub>;

L is a) NR<sup>6</sup>, CR<sup>7</sup>R<sup>8</sup>, -OCR<sup>7</sup>R<sup>8</sup>-, -NR<sup>6</sup>CR<sup>7</sup>R<sup>8</sup>-, or -S(O)<sub>m</sub>CR<sup>7</sup>R<sup>8</sup>-, wherein the L=C bond is a single bond; or

b) CR<sup>7</sup>, wherein the L=C bond is a double bond, with the proviso that D is absent when the L=C bond is a double bond; or

c) absent, wherein C is covalently bonded by a single bond to Ar<sup>1</sup>;

Ar<sup>1</sup> and Ar<sup>2</sup> are each independently mono- or bicyclic aromatic rings of 5-12 atoms, including, but not limited to phenyl, pyridyl, pyrimidyl, pyrazinyl, pyridazinyl, thienyl, furanyl, pyrrolyl, imidazolyl, pyrazolyl, oxazolyl, isoxazolyl, thiazolyl, isothiazolyl, 1,3,4-oxadiazolyl, 1,2,4-oxadiazolyl, 1,3,4-thiadiazolyl, 1,2,3-triazolyl, 1,3,4-triazolyl, 1,2,4-triazinyl, 1,3,5-triazinyl, benzofuranyl, benzothienyl, indolyl, indazolyl, benzimidazolyl, benzoxazolyl, benzoisoxazolyl, benzothiazolyl, benzoisothiazolyl, quinoliny, isoquinoliny, quinazolinyl, quinoxalinyl, naphthyridyl, or purinyl;

Y<sup>1</sup>, Y<sup>2</sup>, and Z<sup>1</sup> are each independently a lone electron pair, H, C<sub>1</sub>-C<sub>6</sub> lower alkyl, C<sub>2</sub>-C<sub>6</sub> lower alkenyl, C<sub>2</sub>-C<sub>6</sub> lower alkynyl, C<sub>1</sub>-C<sub>6</sub> lower alkoxy, C<sub>1</sub>-C<sub>6</sub> lower alkylamino, C<sub>1</sub>-C<sub>6</sub> lower dialkylamino, C<sub>2</sub>-C<sub>6</sub> lower cycloalkyl, C<sub>4</sub>-C<sub>6</sub> lower cycloalkenyl, C<sub>1</sub>-C<sub>6</sub> lower thioalkyl, C<sub>1</sub>-C<sub>6</sub> lower sulfinylalkyl, C<sub>1</sub>-C<sub>6</sub> lower sulfonylalkyl, C<sub>1</sub>-C<sub>6</sub> lower acyloxy, C<sub>1</sub>-C<sub>6</sub> lower acylamino with N substituted with R<sup>6</sup>, CH<sub>2</sub>OR<sup>5</sup>, CH<sub>2</sub>NR<sup>6</sup>R<sup>6a</sup>, R<sub>f</sub>, R<sub>f</sub>O, OH, NH<sub>2</sub>, CN, NO<sub>2</sub>, F, Cl, Br, I, or N<sub>3</sub>;

E is a bond, S(O)<sub>m</sub>, NR<sup>6</sup>, C=O, CO<sub>2</sub>, CONR<sup>6</sup>, O, -OC=O, NR<sup>6</sup>C=O, NR<sup>6</sup>CO<sub>2</sub>, OC=ONR<sup>6</sup>, OCO<sub>2</sub>, or NR<sup>6</sup>CONR<sup>6a</sup>;

F is (CH<sub>2</sub>)<sub>n</sub>, (CH<sub>2</sub>)<sub>o</sub>O(CH<sub>2</sub>)<sub>p</sub>, (CH<sub>2</sub>)<sub>o</sub>NR<sup>6</sup>(CH<sub>2</sub>)<sub>p</sub>, (CH<sub>2</sub>)<sub>o</sub>NR<sup>6</sup>CO(CH<sub>2</sub>)<sub>p</sub>, (CH<sub>2</sub>)<sub>o</sub>CONR<sup>6</sup>(CH<sub>2</sub>)<sub>p</sub>, (CH<sub>2</sub>)<sub>o</sub>(CR<sup>6</sup>=CR<sup>6</sup>)<sub>q</sub>(CH<sub>2</sub>)<sub>p</sub>, (CH<sub>2</sub>)<sub>o</sub>-(C≡C)<sub>q</sub>-(CH<sub>2</sub>)<sub>p</sub>;

G is a bond, O, NR<sup>6</sup>, CO, CO<sub>2</sub>, OCO, OCO<sub>2</sub>, S(O)<sub>m</sub>, CONR<sup>6</sup>, NR<sup>6</sup>CO, NR<sup>6</sup>CO<sub>2</sub>, OCONR<sup>6</sup>, NR<sup>6</sup>CONR<sup>6a</sup>, or G can optionally be attached to Ar<sup>2</sup> at two contiguous C atoms to form a 5- to 7-membered partially saturated ring, which contains 0, 1, or 2 heteroatoms selected from the group consisting of O, N, and S;

X, X<sup>1</sup> are independently O or S

Z<sup>2</sup> is nothing, H or Ar<sup>1</sup> optionally substituted with Y<sup>1</sup> and Y<sup>2</sup>;

- $R^1$ ,  $R^2$ ,  $R^3$ , and  $R^4$ , are each independently selected from H, C<sub>1</sub>-C<sub>6</sub> lower alkyl, C<sub>3</sub>-C<sub>6</sub> lower alkenyl, C<sub>3</sub>-C<sub>6</sub> lower alkynyl, C<sub>3</sub>-C<sub>6</sub> lower cycloalkyl, C<sub>4</sub>-C<sub>6</sub> lower cycloalkenyl, or independently  $R^1$  and  $R^2$  or  $R^3$  and  $R^4$  can be taken together to form a 5 to 8-membered ring containing 2-7 carbon atoms, the 5 to 8-membered ring optionally substituted with zero to 3 substituents selected from the group C<sub>1</sub>-C<sub>4</sub> lower alkyl, C<sub>1</sub>-C<sub>4</sub> lower alkoxy, C<sub>1</sub>-C<sub>4</sub> lower alkylamino, C<sub>1</sub>-C<sub>4</sub> lower dialkylamino, amino, hydroxyl, hydroxymethyl, methoxymethyl, phenyl, substituted phenyl, benzyl, substituted benzyl;
- U and V are each independently a bond, O or NR<sup>6</sup>;
- $R^5$ ,  $R^6$  and  $R^{6a}$  are each independently C<sub>1</sub>-C<sub>6</sub> alkyl, C<sub>3</sub>-C<sub>6</sub> cycloalkyl, C<sub>3</sub>-C<sub>6</sub> alkenyl, C<sub>3</sub>-C<sub>6</sub> cycloalkenyl, C<sub>3</sub>-C<sub>6</sub> alkynyl, and H;
- $R^7$  and  $R^8$  are each independently H, C<sub>1</sub>-C<sub>4</sub> lower alkyl, or are taken together to form a saturated C<sub>3</sub>-C<sub>6</sub> carbocyclic ring;
- $R_f$  is C<sub>1</sub>-C<sub>4</sub> straight or branched lower perfluoroalkyl;
- all lower alkyl, alkenyl and alkynyl groups including those linked via heteroatoms can be straight chain or branched;
- m is 0, 1, or 2;
- n is 0, 1, 2, 3, 4, 5, or 6;
- o is 0, 1, 2, 3, 4, 5, or 6;
- p is 0, 1, 2, 3, 4, 5, or 6; and
- q is 0, 1, 2, 3, 4, 5, or 6.

The present invention also relates to pharmaceutical formulations comprising a compound of Formula (I), or a pharmaceutically acceptable salt thereof, in combination with a pharmaceutically acceptable carrier, excipient, solvent, adjuvant or diluent.



The present invention further relates to methods of regulating HDL and/or LDL cholesterol levels in a subject comprising administering to a subject a compound, or pharmaceutical formulation comprising a compound, of Formula (I) or pharmaceutically acceptable salt thereof.

- 5           The invention relates to methods of lowering blood triglyceride and/or glucose levels in a subject comprising administering to a subject in need of such treatment an effective amount of a compound, or pharmaceutical formulation comprising a compound, of Formula (I) or pharmaceutically acceptable salt thereof.

- 10           The invention also relates to methods of treating disease states related to blood levels of HDL/LDL levels, triglycerides, and/or glucose in a mammal comprising administering to a mammal in need of such treatment a therapeutically effective amount of a compound, or pharmaceutical formulation comprising a compound, of Formula (I), or pharmaceutically acceptable salt thereof.

## **DETAILED DESCRIPTION OF THE INVENTION**

15   Definitions

Unless defined otherwise, all scientific and technical terms used herein have the same meaning as commonly understood by one of skill in the art to which this invention belongs.

- 20           All patents and publications referred to herein are hereby incorporated by reference for all purposes.

A "therapeutically effective" amount is defined as an amount effective to reduce or lessen at least one symptom of the disease being treated or to reduce or delay onset of one or more clinical markers or symptoms of the disease.

- 25           As used in this specification and the appended claims, the singular forms "a," "an," and "the" include plural referents unless the content clearly dictates otherwise.

Thus, for example, reference to a composition containing "a compound" includes a mixture of two or more compounds. It should also be noted that the term "or" is generally employed in its sense including "and/or" unless the content clearly dictates otherwise.

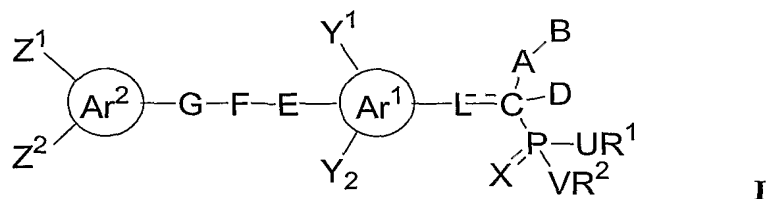
5 By "alkyl" and "C<sub>1</sub>-C<sub>6</sub> alkyl" in the present invention is meant straight or branched chain alkyl groups having 1-6 carbon atoms, such as, methyl, ethyl, propyl, isopropyl, n-butyl, sec-butyl, tert-butyl, pentyl, 2-pentyl, isopentyl, neopentyl, hexyl, 2-hexyl, 3-hexyl, and 3-methylpentyl. It is understood that in cases where an alkyl chain of a substituent (e.g. of an alkyl, alkoxy or alkenyl group) is shorter or longer than 6  
10 carbons, it will be so indicated in the second "C" as, for example, "C<sub>1</sub>-C<sub>10</sub>" indicates a maximum of 10 carbons.

By the term "halogen" in the present invention is meant fluorine, bromine, chlorine, and iodine.

"Alkenyl" and "C<sub>2</sub>-C<sub>6</sub> alkenyl" means straight and branched hydrocarbon groups  
15 having from 2 to 6 carbon atoms and from one to three double bonds and includes, for example, ethenyl, propenyl, 1-but-3-enyl, 1-pent-3-enyl, 1-hex-5-enyl and the like.

As used herein, the term "cycloalkyl" refers to saturated carbocyclic groups having three to twelve carbon atoms. The cycloalkyl can be monocyclic, or a polycyclic fused system. Examples of such groups include cyclopropyl, cyclobutyl, cyclopentyl and  
20 cyclohexyl. The cycloalkyl groups herein are unsubstituted or, as specified, substituted in one or more substitutable positions with various groups. For example, such cycloalkyl groups may be optionally substituted with, for example, C<sub>1</sub>-C<sub>6</sub> alkyl, C<sub>1</sub>-C<sub>6</sub> alkoxy, halogen, hydroxy, cyano, nitro, amino, mono(C<sub>1</sub>-C<sub>6</sub>)alkylamino, di(C<sub>1</sub>-C<sub>6</sub>)alkylamino, C<sub>2</sub>-C<sub>6</sub>alkenyl, C<sub>2</sub>-C<sub>6</sub>alkynyl, C<sub>1</sub>-C<sub>6</sub> haloalkyl, C<sub>1</sub>-C<sub>6</sub> haloalkoxy, amino(C<sub>1</sub>-C<sub>6</sub>)alkyl,  
25 mono(C<sub>1</sub>-C<sub>6</sub>)alkylamino(C<sub>1</sub>-C<sub>6</sub>)alkyl or di(C<sub>1</sub>-C<sub>6</sub>)alkylamino(C<sub>1</sub>-C<sub>6</sub>)alkyl.

In one aspect, the present invention relates to phosphorus-containing compounds of Formula (I):



wherein

- 5        A is a bond, O, CH<sub>2</sub>, CHF, CF<sub>2</sub>, or NR<sub>6</sub>;
- B is H, C<sub>1</sub>-C<sub>6</sub> lower alkyl, or P(=X<sup>1</sup>)(UR<sup>3</sup>)(VR<sup>4</sup>);
- D is    a) H or lower alkyl, wherein the L=C bond is a single bond; or  
               b) OH, OCOR<sup>5</sup>, NH<sub>2</sub>, NR<sup>6</sup>R<sup>6a</sup>, or NHCOR<sup>5</sup>, wherein the L=C bond is a single bond, with the proviso that A is CH<sub>2</sub>, CHF, CF<sub>2</sub>;
- 10       L is    a) NR<sup>6</sup>, CR<sup>7</sup>R<sup>8</sup>, -OCR<sup>7</sup>R<sup>8</sup>-, -NR<sup>6</sup>CR<sup>7</sup>R<sup>8</sup>-, or -S(O)<sub>m</sub>CR<sup>7</sup>R<sup>8</sup>-, wherein the L=C bond is a single bond; or  
               b) CR<sup>7</sup>, wherein the L=C bond is a double bond, with the proviso that D is absent when the L=C bond is a double bond; or  
               c) absent, wherein C is covalently bonded by a single bond to Ar<sup>1</sup>;
- 15       Ar<sup>1</sup> and Ar<sup>2</sup> are each independently mono- or bicyclic aromatic rings of 5-12 atoms, including, but not limited to phenyl, pyridyl, pyrimidyl, pyrazinyl, pyridazinyl, thienyl, furanyl, pyrrolyl, imidazyl, pyrazolyl, oxazolyl, isoxoazolyl, thiazolyl, isothiazolyl, 1,3,4-oxadiazolyl, 1,2,4-oxadiazolyl, 1,3,4-thiadiazolyl, 1,2,3-triazolyl, 1,3,4-triazolyl, 1,2,4-triazinyl, 1,3,5-triazinyl, benzofuranyl,
- 20       benzothienyl, indolyl, indazolyl, benzimidazyl, benzoxazolyl, benzoisoxazolyl, benzothiazolyl, benzoisothiazolyl, quinolinyl, isoquinolinyl, quinazolinyl, quinoxalinyl, naphthyridyl, or purinyl;

- Y<sup>1</sup>, Y<sup>2</sup>, and Z<sup>1</sup> are each independently a lone electron pair, H, C<sub>1</sub>-C<sub>6</sub> lower alkyl, C<sub>2</sub>-C<sub>6</sub> lower alkenyl, C<sub>2</sub>-C<sub>6</sub> lower alkynyl, C<sub>1</sub>-C<sub>6</sub> lower alkoxy, C<sub>1</sub>-C<sub>6</sub> lower alkylamino, C<sub>1</sub>-C<sub>6</sub> lower dialkylamino, C<sub>2</sub>-C<sub>6</sub> lower cycloalkyl, C<sub>4</sub>-C<sub>6</sub> lower cycloalkenyl, C<sub>1</sub>-C<sub>6</sub> lower thioalkyl, C<sub>1</sub>-C<sub>6</sub> lower sulfinylalkyl, C<sub>1</sub>-C<sub>6</sub> lower sulfonylalkyl, C<sub>1</sub>-C<sub>6</sub> lower acyloxy, C<sub>1</sub>-C<sub>6</sub> lower acylamino with N substituted with R<sup>6</sup>, CH<sub>2</sub>OR<sup>5</sup>, CH<sub>2</sub>NR<sup>6</sup>R<sup>6a</sup>, R<sub>f</sub>, R<sub>f</sub>O, OH, NH<sub>2</sub>, CN, NO<sub>2</sub>, F, Cl, Br, I, or N<sub>3</sub>;
- E is a bond, S(O)<sub>m</sub>, NR<sup>6</sup>, C=O, CO<sub>2</sub>, CONR<sup>6</sup>, O, -OC=O, NR<sup>6</sup>C=O, NR<sup>6</sup>CO<sub>2</sub>, OC=ONR<sup>6</sup>, OCO<sub>2</sub>, or NR<sup>6</sup>CONR<sup>6a</sup>;
- F is (CH<sub>2</sub>)<sub>n</sub>, (CH<sub>2</sub>)<sub>o</sub>O(CH<sub>2</sub>)<sub>p</sub>, (CH<sub>2</sub>)<sub>o</sub>NR<sup>6</sup>(CH<sub>2</sub>)<sub>p</sub>, (CH<sub>2</sub>)<sub>o</sub>NR<sup>6</sup>CO(CH<sub>2</sub>)<sub>p</sub>, (CH<sub>2</sub>)<sub>o</sub>CONR<sup>6</sup>(CH<sub>2</sub>)<sub>p</sub>, (CH<sub>2</sub>)<sub>o</sub>(CR<sup>6</sup>=CR<sup>6</sup>)<sub>q</sub>(CH<sub>2</sub>)<sub>p</sub>, (CH<sub>2</sub>)<sub>o</sub>-(C≡C)<sub>q</sub>-(CH<sub>2</sub>)<sub>p</sub>;
- G is a bond, O, NR<sup>6</sup>, CO, CO<sub>2</sub>, OCO, OCO<sub>2</sub>, S(O)<sub>m</sub>, CONR<sup>6</sup>, NR<sup>6</sup>CO, NR<sup>6</sup>CO<sub>2</sub>, OCONR<sup>6</sup>, NR<sup>6</sup>CONR<sup>6a</sup>, or G can optionally be attached to Ar<sup>2</sup> at two contiguous C atoms to form a 5- to 7-membered partially saturated ring, which contains 0, 1, or 2 heteroatoms selected from the group consisting of O, N, and S;
- X, X<sup>1</sup> are independently O or S
- Z<sup>2</sup> is nothing, H or Ar<sup>1</sup> optionally substituted with Y<sup>1</sup> and Y<sup>2</sup>;
- R<sup>1</sup>, R<sup>2</sup>, R<sup>3</sup>, and R<sup>4</sup>, are each independently selected from H, C<sub>1</sub>-C<sub>6</sub> lower alkyl, C<sub>3</sub>-C<sub>6</sub> lower alkenyl, C<sub>3</sub>-C<sub>6</sub> lower alkynyl, C<sub>3</sub>-C<sub>6</sub> lower cycloalkyl, C<sub>4</sub>-C<sub>6</sub> lower cycloalkenyl, or independently R<sup>1</sup> and R<sup>2</sup> or R<sup>3</sup> and R<sup>4</sup> can be taken together to form a 5 to 8-membered ring containing 2-7 carbon atoms, the 5 to 8-membered ring optionally substituted with zero to 3 substituents selected from the group C<sub>1</sub>-C<sub>4</sub> lower alkyl, C<sub>1</sub>-C<sub>4</sub> lower alkoxy, C<sub>1</sub>-C<sub>4</sub> lower alkylamino, C<sub>1</sub>-C<sub>4</sub> lower dialkylamino, amino, hydroxyl, hydroxymethyl, methoxymethyl, phenyl, substituted phenyl, benzyl, substituted benzyl;
- U and V are each independently a bond, O or NR<sup>6</sup>;

$R^5$ ,  $R^6$  and  $R^{6a}$  are each independently  $C_1$ - $C_6$  alkyl,  $C_3$ - $C_6$  cycloalkyl,  $C_3$ - $C_6$  alkenyl,  $C_3$ - $C_6$  cycloalkenyl,  $C_3$ - $C_6$  alkynyl, and H;

$R^7$  and  $R^8$  are each independently H,  $C_1$ - $C_4$  lower alkyl, or are taken together to form a saturated  $C_3$ - $C_6$  carbocyclic ring;

5  $R_f$  is  $C_1$ - $C_4$  straight or branched lower perfluoroalkyl;

all lower alkyl, alkenyl and alkynyl groups including those linked via heteroatoms can be straight chain or branched;

m is 0, 1, or 2;

n is 0, 1, 2, 3, 4, 5, or 6;

10 o is 0, 1, 2, 3, 4, 5, or 6;

p is 0, 1, 2, 3, 4, 5, or 6; and

q is 0, 1, 2, 3, 4, 5, or 6;

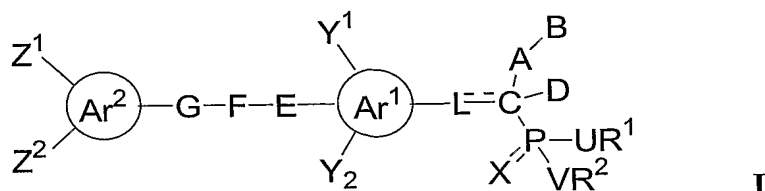
or a pharmaceutically acceptable salt thereof.

In one embodiment of this aspect, the compound is of Formula (I), wherein A is  
15 selected from a bond, O, and  $CH_2$ ; B is  $P(=O)(UR^3)(VR^4)$ ; D is H; and the  $L \equiv C$  bond is a single bond.

In a further embodiment of this aspect, the compound is of Formula (I), wherein A is selected from a bond, O, and  $CH_2$ ; B is  $P(=O)(UR^3)(VR^4)$ ; D is H; the  $L \equiv C$  bond is a single bond; and  $Ar^1$  is phenyl.

20 In yet a further embodiment of this aspect, the compound is of Formula (I), wherein A is selected from a bond, O, and  $CH_2$ ; B is  $P(=O)(UR^3)(VR^4)$ ; D is H; the  $L \equiv C$  bond is a single bond;  $Ar^1$  is phenyl; and U and V are each O.

In a preferred embodiment, the invention provides phosphorus-containing compounds of Formula (I):



wherein

A is a bond, O, CH<sub>2</sub>, CHF, CF<sub>2</sub>, or NR<sub>6</sub>;

B is H, C<sub>1</sub>-C<sub>6</sub> lower alkyl, or P(=X<sup>1</sup>)(UR<sup>3</sup>)(VR<sup>4</sup>);

- 5 D is a) H or lower alkyl, wherein the L=C bond is a single bond; or
- b) OH, OCOR<sup>5</sup>, NH<sub>2</sub>, NR<sup>6</sup>R<sup>6a</sup>, or NHCOR<sup>5</sup>, wherein the L=C bond is a single bond, with the proviso that A is CH<sub>2</sub>, CHF, CF<sub>2</sub>;
- L is a) NR<sup>6</sup>, CR<sup>7</sup>R<sup>8</sup>, -OCR<sup>7</sup>R<sup>8</sup>-, -NR<sup>6</sup>CR<sup>7</sup>R<sup>8</sup>-, or -S(O)<sub>m</sub>CR<sup>7</sup>R<sup>8</sup>-, wherein the L=C bond is a single bond; or
- 10 b) CR<sup>7</sup>, wherein the L=C bond is a double bond, with the proviso that D is absent when the L=C bond is a double bond; or
- c) absent, wherein C is covalently bonded by a single bond to Ar<sup>1</sup>;

Ar<sup>1</sup> and Ar<sup>2</sup> are each independently mono- or bicyclic aromatic rings of 5-12 atoms, including, but not limited to phenyl, pyridyl, pyrimidyl, pyrazinyl, pyridazinyl,

15 thienyl, furanyl, pyrrolyl, imidazyl, pyrazolyl, oxazolyl, isoxoazolyl, thiazolyl, isothiazolyl, 1,3,4-oxadiazolyl, 1,2,4-oxadiazolyl, 1,3,4-thiadiazolyl, 1,2,3-triazolyl, 1,3,4-triazolyl, 1,2,4-triazinyl, 1,3,5-triazinyl, benzofuranyl, benzothienyl, indolyl, indazolyl, benzimidazyl, benzoxazolyl, benzoisoxazolyl, benzothiazolyl, benzoisothiazolyl, quinoliny, isoquinoliny, quinazoliny,

20 quinoxaliny, naphthyridyl, or puriny;

Y<sup>1</sup>, Y<sup>2</sup>, and Z<sup>1</sup> are each independently a lone electron pair, H, C<sub>1</sub>-C<sub>6</sub> lower alkyl, C<sub>2</sub>-C<sub>6</sub> lower alkenyl, C<sub>2</sub>-C<sub>6</sub> lower alkynyl, C<sub>1</sub>-C<sub>6</sub> lower alkoxy, C<sub>1</sub>-C<sub>6</sub> lower

alkylamino, C<sub>1</sub>-C<sub>6</sub> lower dialkylamino, C<sub>2</sub>-C<sub>6</sub> lower cycloalkyl, C<sub>4</sub>-C<sub>6</sub> lower cycloalkenyl, C<sub>1</sub>-C<sub>6</sub> lower thioalkyl, C<sub>1</sub>-C<sub>6</sub> lower sulfinylalkyl, C<sub>1</sub>-C<sub>6</sub> lower sulfonylalkyl, C<sub>1</sub>-C<sub>6</sub> lower acyloxy, C<sub>1</sub>-C<sub>6</sub> lower acylamino with N substituted with R<sup>6</sup>, CH<sub>2</sub>OR<sup>5</sup>, CH<sub>2</sub>NR<sup>6</sup>R<sup>6a</sup>, R<sub>f</sub>, R<sub>f</sub>O, OH, NH<sub>2</sub>, CN, NO<sub>2</sub>, F, Cl, Br, I, or N<sub>3</sub>;

5 E is a bond, S(O)<sub>m</sub>, NR<sup>6</sup>, C=O, CO<sub>2</sub>, CONR<sup>6</sup>, O, -OC=O, NR<sup>6</sup>C=O, NR<sup>6</sup>CO<sub>2</sub>, OC=ONR<sup>6</sup>, OCO<sub>2</sub>, or NR<sup>6</sup>CONR<sup>6a</sup>;

F is (CH<sub>2</sub>)<sub>n</sub>, (CH<sub>2</sub>)<sub>o</sub>O(CH<sub>2</sub>)<sub>p</sub>, (CH<sub>2</sub>)<sub>o</sub>NR<sup>6</sup>(CH<sub>2</sub>)<sub>p</sub>, (CH<sub>2</sub>)<sub>o</sub>NR<sup>6</sup>CO(CH<sub>2</sub>)<sub>p</sub>, (CH<sub>2</sub>)<sub>o</sub>CONR<sup>6</sup>(CH<sub>2</sub>)<sub>p</sub>, (CH<sub>2</sub>)<sub>o</sub>(CR<sup>6</sup>=CR<sup>6</sup>)<sub>q</sub>(CH<sub>2</sub>)<sub>p</sub>, (CH<sub>2</sub>)<sub>o</sub>-(C≡C)<sub>q</sub>-(CH<sub>2</sub>)<sub>p</sub>;

G is a bond, O, NR<sup>6</sup>, CO, CO<sub>2</sub>, OCO, OCO<sub>2</sub>, S(O)<sub>m</sub>, CONR<sup>6</sup>, NR<sup>6</sup>CO, NR<sup>6</sup>CO<sub>2</sub>,  
 10 OCONR<sup>6</sup>, NR<sup>6</sup>CONR<sup>6a</sup>, or G can optionally be attached to Ar<sup>2</sup> at two contiguous C atoms to form a 5- to 7-membered partially saturated ring, which contains 0, 1, or 2 heteroatoms selected from the group consisting of O, N, and S;

X, X<sup>1</sup> are independently O or S

Z<sup>2</sup> is nothing, H or Ar<sup>1</sup> optionally substituted with Y<sup>1</sup> and Y<sup>2</sup>;

15 R<sup>1</sup>, R<sup>2</sup>, R<sup>3</sup>, and R<sup>4</sup>, are each independently selected from H, C<sub>1</sub>-C<sub>6</sub> lower alkyl, C<sub>3</sub>-C<sub>6</sub> lower alkenyl, C<sub>3</sub>-C<sub>6</sub> lower alkynyl, C<sub>3</sub>-C<sub>6</sub> lower cycloalkyl, C<sub>4</sub>-C<sub>6</sub> lower cycloalkenyl, or independently R<sup>1</sup> and R<sup>2</sup> or R<sup>3</sup> and R<sup>4</sup> can be taken together to form a 5 to 8-membered ring containing 2-7 carbon atoms, the 5 to 8-membered ring optionally substituted with zero to 3 substituents selected from the group C<sub>1</sub>-  
 20 C<sub>4</sub> lower alkyl, C<sub>1</sub>-C<sub>4</sub> lower alkoxy, C<sub>1</sub>-C<sub>4</sub> lower alkylamino, C<sub>1</sub>-C<sub>4</sub> lower dialkylamino, amino, hydroxyl, hydroxymethyl, methoxymethyl, phenyl, substituted phenyl, benzyl, substituted benzyl;

U and V are each independently a bond, O or NR<sup>6</sup>;

R<sup>5</sup> R<sup>6</sup> and R<sup>6a</sup> are each independently C<sub>1</sub>-C<sub>6</sub> alkyl, C<sub>3</sub>-C<sub>6</sub> cycloalkyl, C<sub>3</sub>-C<sub>6</sub> alkenyl,  
 25 C<sub>3</sub>-C<sub>6</sub> cycloalkenyl, C<sub>3</sub>-C<sub>6</sub> alkynyl, and H;

$R^7$  and  $R^8$  are each independently H, C<sub>1</sub>-C<sub>4</sub> lower alkyl, or are taken together to form a saturated C<sub>3</sub>-C<sub>6</sub> carbocyclic ring;

$R_f$  is C<sub>1</sub>-C<sub>4</sub> straight or branched lower perfluoroalkyl;

all lower alkyl, alkenyl and alkynyl groups including those linked via heteroatoms can  
5 be straight chain or branched;

m is 0, 1, or 2;

n is 0, 1, 2, 3, 4, 5, or 6;

o is 0, 1, 2, 3, 4, 5, or 6;

p is 0, 1, 2, 3, 4, 5, or 6; and

10 q is 0, 1, 2, 3, 4, 5, or 6;

with the provisos that

when A is a bond or O, B is P(O)(OR<sup>3</sup>)(OR<sup>4</sup>), and D is selected from the group H, OH, OCOCH<sub>3</sub>, and NH<sub>2</sub>, and when  $R^1 = R^2$  and  $R^3 = R^4$ , and both are selected from the group H or unsubstituted C<sub>1</sub>-C<sub>4</sub> lower alkyl, and E and G are bonds, and F is  
15 (CH<sub>2</sub>)<sub>n</sub> where n is 0, and both Ar<sup>1</sup> and Ar<sup>2</sup> are phenyl, then at least one of Y<sup>1</sup>, Y<sup>2</sup>, Z<sup>1</sup>, or Z<sup>2</sup> must not be H; and

when A is a bond or CH<sub>2</sub>, and B is P(O)(OR<sup>3</sup>)(OR<sup>4</sup>), and either D is H or C<sub>1</sub>-C<sub>4</sub> lower alkyl where L is CH<sub>2</sub>, or D is absent, with L≡C taken together represent an ethenylidene group, and Ar<sup>1</sup> is phenyl, and E is a bond or O, and  $R^1 = R^2$  and  $R^3 = R^4$ ,  
20 and both are drawn from the group H or C<sub>1</sub>-C<sub>6</sub> unsubstituted lower alkyl, then one of Y<sup>1</sup> and Y<sup>2</sup> must be other than H or unsubstituted C<sub>1</sub>-C<sub>4</sub> lower alkyl or unsubstituted C<sub>1</sub>-C<sub>4</sub> lower alkoxy; and

when A is O, and B is H or P(O)(OR<sup>3</sup>)(OR<sup>4</sup>), and R<sup>1</sup>, R<sup>2</sup>, R<sup>3</sup>, and R<sup>4</sup> are all selected from the group H or C<sub>1</sub>-C<sub>6</sub> unsubstituted lower alkyl, and D is H, and L is a  
25 bond, and Ar<sup>1</sup> is phenyl, and E is other than a bond or O, then one of Y<sup>1</sup> or Y<sup>2</sup> must



be other than H, or C<sub>1</sub>-C<sub>4</sub> unsubstituted lower alkyl or C<sub>1</sub>-C<sub>4</sub> unsubstituted lower alkoxy;

or a pharmaceutically acceptable salt thereof.

In a more preferred embodiment, the compound of Formula (I) is selected from:

- 5 Diethyl 1-(diethoxyphosphinyloxy)-1-(4-[2-{*N*-methyl-*N*-pyrid-2-ylamino}ethoxy]-3-fluorophenyl)methylphosphonate;
- Diethyl 1-(diethoxyphosphinyloxy)-1-(4-[*N*-(2-{*N*-methyl-*N*-pyrid-2-ylamino}ethyl)-*N*-methylaminocarbonyl]-3-fluorophenyl)methylphosphonate;
- Diethyl 1-(diethoxyphosphinyloxy)-1-(4-[3-{*N*-methyl-*N*-pyrid-2-ylamino}-1-oxoprop-1-yl]-3-fluorophenyl)methylphosphonate;
- 10 Diethyl 1-(diethoxyphosphinyloxy)-1-(4-[2-{5-methyl-2-phenyloxazol-4-yl}ethoxy]-3-fluorophenyl)methylphosphonate;
- Diethyl 1-(diethoxyphosphinyloxy)-1-(4-[*N*-(2-{5-methyl-2-phenyloxazol-4-yl}ethyl)-*N*-methylaminocarbonyl]-3-fluorophenyl)methylphosphonate;
- 15 Diethyl 1-(diethoxyphosphinyloxy)-1-(4-[2-{5-methyl-2-phenylthiazol-4-yl}ethoxy]-3-fluorophenyl)methylphosphonate;
- Diethyl 1-(diethoxyphosphinyloxy)-1-(4-[3-{5-methyl-2-phenylthiazol-4-yl}-1-oxoprop-1-yl]-3-fluorophenyl)methylphosphonate;
- Diethyl 1-(diethoxyphosphinyloxy)-1-(4-[2-{5-methyl-2-pyrid-4-ylloxazol-4-yl}ethoxy]-3-fluorophenyl)methylphosphonate;
- 20 Diethyl 1-(diethoxyphosphinyloxy)-1-(4-[2-{5-methyl-2-pyrid-4-ylthiazol-4-yl}ethoxy]-3-fluorophenyl)methylphosphonate;
- Diethyl 1-(diethoxyphosphinyloxy)-1-(4-[3-{5-methyl-2-pyrid-4-ylloxazol-4-yl}-1-oxoprop-1-yl]-3-fluorophenyl)methylphosphonate;

- Diethyl 1-(hydroxy)-1-(4-[*N*-(2-{5-methyl-2-pyrid-4-ylthiazol-4-yl} ethyl)-*N*-methylaminocarbonyl]-3-fluorophenyl)methylphosphonate;
- Diethyl 1-(hydroxy)-1-(4-[2-{4-(4-trifluoromethylphenyl)phenoxy} ethoxy]-3-fluorophenyl)methylphosphonate;
- 5 Diethyl 1-(hydroxy)-1-(4-[*N*-(2-{4-(4-trifluoromethylphenyl)phenoxy} ethyl)-*N*-methylaminocarbonyl]-3-fluorophenyl)methylphosphonate;
- Diethyl 1-(hydroxy)-1-(4-[3-{4-(4-trifluoromethylphenyl)phenoxy}-1-oxoprop-1-yl]-3-fluorophenyl)methylphosphonate;
- Diethyl 1-(hydroxy)-1-(4-[2-{1-[4-(2-trifluoromethylphenyl)phenylmethyl]-3-hexylureido} ethyl]-3-fluorophenyl)methylphosphonate;
- 10 Diethyl 1-(hydroxy)-1-(4-[2-{1-butyl-3-(5-methoxypyrid-2-yl)ureido} ethyl]-3-fluorophenyl)methylphosphonate;
- Diethyl 1-(hydroxy)-1-(4-[3-{4-acetyl-3-hydroxy-2-propylphenoxy} propoxy]-3-fluorophenyl)methylphosphonate;
- 15 Diethyl 1-(hydroxy)-1-(4-[2-{4*H*-3-oxobenzo[1,4]oxazin-2-yl} ethoxy]-3-fluorophenyl)methylphosphonate;
- Diethyl 1-(hydroxy)-1-(4-[3,*N*-phthalimidopropoxy]-3-fluorophenyl)methylphosphonate;
- Diethyl 1-(hydroxy)-1-(4-[4,*N*-phthalimidobutoxy]-3-fluorophenyl)methylphosphonate;
- Tetraethyl 1-(3-[3-{*N*-methyl-*N*-pyrid-2-ylamino} propoxy]-4-fluorophenyl
- 20 )methylidenebisphosphonate;
- Tetraethyl 1-(3-[*N*-(3-{*N*-methyl-*N*-pyrid-2-ylamino} propyl)-*N*-methylamino]-4-fluorophenyl)methylidenebisphosphonate;
- Tetraethyl 1-(3-[3-{*N*-methyl-*N*-pyrid-2-ylamino}-1-oxoprop-1-ylamino]-4-fluorophenyl)methylidenebisphosphonate;

- Tetraethyl 1-(3-[3-{5-methyl-2-phenyloxazol-4-yl}propoxy]-4-fluorophenyl)methylidenebisphosphonate;
- Tetraethyl 1-(3-[*N*-(2-{5-methyl-2-phenyloxazol-4-yl}ethyl)-*N*-methylaminocarbonyl]-4-methoxyphenyl)methylidenebisphosphonate;
- 5 Tetraethyl 1-(3-[3-{5-methyl-2-phenylthiazol-4-yl}propoxy]-4-fluorophenyl)methylidenebisphosphonate;
- Tetraethyl 1-(3-[3-{5-methyl-2-phenylthiazol-4-yl}-1-oxoprop-1-yl]-4-fluorophenyl)methylidenebisphosphonate;
- Tetraethyl 1-(3-[4-{5-methyl-2-pyrid-4-yloxazol-4-yl}butoxy]-4-fluorophenyl)methylidenebisphosphonate;
- 10 Tetraethyl 1-(3-[3-{5-methyl-2-pyrid-4-ylthiazol-4-yl}propoxy]-4-fluorophenyl)methylidenebisphosphonate;
- Tetraethyl 1-(3-[3-{5-methyl-2-pyrid-4-yloxazol-4-yl}-1-oxoprop-1-ylthio]-4-fluorophenyl)methylidenebisphosphonate;
- 15 Tetraethyl 2-(3-[*N*-(3-{5-methyl-2-pyrid-4-ylthiazol-4-yl}propyl)-*N*-methylamino]-4-fluorophenyl)vinylidene-1,1-bisphosphonate;
- Tetraethyl 2-(3-[3-{4-(4-trifluoromethylphenyl)phenoxy}propoxy]-4-fluorophenyl)vinylidene-1,1-bisphosphonate;
- Tetraethyl 2-(3-[*N*-(3-{4-(4-trifluoromethylphenyl)phenoxy}propyl)-*N*-methylamino]-4-fluorophenyl)vinylidene-1,1-bisphosphonate;
- 20 Tetraethyl 2-(3-[4-{4-(4-trifluoromethylphenyl)phenoxy}-1-oxobut-1-yl]-4-fluorophenyl)vinylidene-1,1-bisphosphonate;
- Tetraethyl 2-(3-[2-{1-[4-(2-trifluoromethylphenyl)phenylmethyl]-3-hexylureido}ethyl]-4-fluorophenyl)vinylidene-1,1-bisphosphonate;

- Tetraethyl 2-(3-[2-{1-butyl-3-(5-methoxypyrid-2-yl)ureido}ethyl]-4-fluorophenyl)vinylidene-1,1-bisphosphonate;
- Tetraethyl 2-(3-[4-{4-acetyl-3-hydroxy-2-propylphenoxy}butoxy]-4-fluorophenyl)vinylidene-1,1-bisphosphonate;
- 5 Tetraethyl 2-(3-[3-{4*H*-3-oxobenzo[1,4]oxazin-2-yl}propoxy]-4-fluorophenyl)vinylidene-1,1-bisphosphonate;
- Tetraethyl 2-(3-[3,*N*-phthalimidopropoxy]-4-fluorophenyl)vinylidene-1,1-bisphosphonate;
- Tetraethyl 2-(3-[4,*N*-phthalimidobutoxy]-4-fluorophenyl)vinylidene-1,1-bisphosphonate;
- Tetraethyl 1-(6-[2-{*N*-methyl-*N*-pyrid-2-ylamino}ethoxy]indol-2-yl)ethylidene-1,2-
- 10 bisphosphonate;
- Tetraethyl 1-(6-[*N*-(2-{*N*-methyl-*N*-pyrid-2-ylamino}ethyl)-*N*-methylanino]indol-2-yl)ethylidene-1,2-bisphosphonate;
- Tetraethyl 1-(6-[3-{*N*-methyl-*N*-pyrid-2-ylamino}-1-oxoprop-1-yl]indol-2-yl)ethylidene-1,2-bisphosphonate;
- 15 Tetraethyl 1-(6-[2-{5-methyl-2-phenyloxazol-4-yl}ethoxy] indol-2-yl)ethylidene-1,2-bisphosphonate;
- Tetraethyl 1-(6-[*N*-(2-{5-methyl-2-phenyloxazol-4-yl}ethyl)-*N*-methylanino] indol-2-yl)ethylidene-1,2-bisphosphonate;
- Tetraethyl 1-(6-[2-{5-methyl-2-phenylthiazol-4-yl}ethoxy]indol-2-yl)ethylidene-1,2-
- 20 bisphosphonate;
- Tetraethyl 1-(6-[3-{5-methyl-2-phenylthiazol-4-yl}-1-oxoprop-1-yl]indol-2-yl)ethylidene-1,2-bisphosphonate;
- Tetraethyl 1-(6-[2-{5-methyl-2-pyrid-4-yloxazol-4-yl}ethoxy]indol-2-yl)ethylidene-1,2-bisphosphonate;

- Tetraethyl 1-(6-[2-{5-methyl-2-pyrid-4-ylthiazol-4-yl}ethoxy]indol-2-yl)ethylidene-1,2-bisphosphonate;
- Tetraethyl 1-(6-[3-{5-methyl-2-pyrid-4-yloxazol-4-yl}-1-oxoprop-1-yl]indol-2-yl)ethylidene-1,2-bisphosphonate;
- 5 Tetraethyl 2-(6-[*N*-(2-{5-methyl-2-pyrid-4-ylthiazol-4-yl}ethyl)-*N*-methylamino]indol-2-yl)ethylidene-1,1-bisphosphonate;
- Tetraethyl 2-(6-[2-{4-(4-trifluoromethylphenyl)phenoxy}ethoxy] indol-2-yl)ethylidene-1,1-bisphosphonate;
- Tetraethyl 2-(6-[*N*-(2-{4-(4-trifluoromethylphenyl)phenoxy}ethyl)-*N*-methylamino]indol-10 2-yl)ethylidene-1,1-bisphosphonate;
- Tetraethyl 2-(6-[2-{1-[4-(2-trifluoromethylphenyl)phenylmethyl]-3-hexylureido}ethyl]indol-2-yl)ethylidene-1,1-bisphosphonate;
- Tetraethyl 2-(6-[2-{1-butyl-3-(5-methoxypyrid-2-yl)ureido}ethyl]indol-2-yl)ethylidene-1,1-bisphosphonate;
- 15 Tetraethyl 2-(6-[3-{4-(4-trifluoromethylphenyl)phenoxy}-1-oxoprop-1-yl]indol-2-yl)ethylidene-1,1-bisphosphonate;
- Tetraethyl 2-(6-[3-{4-acetyl-3-hydroxy-2-propylphenoxy}propoxy]indol-2-yl)ethylidene-1,1-bisphosphonate;
- Tetraethyl 2-(6-[2-{4*H*-3-oxobenzo[1,4]oxazin-2-yl}ethoxy]indol-2-yl)ethylidene-1,1-20 bisphosphonate;
- Tetraethyl 2-(6-[3,*N*-phthalimidopropoxy]indol-2-yl)ethylidene-1,1-bisphosphonate;
- Tetraethyl 2-(6-[4,*N*-phthalimidobutoxy]indol-2-yl)ethylidene-1,1-bisphosphonate;
- Tetraethyl *N*-(5-[2-{*N*-methyl-*N*-pyrid-2-ylamino}ethoxy]pyrid-2-yl)aminomethylidenebisphosphonate;

- Tetraethyl *N*-(5-[*N*-(2-{*N*-methyl-*N*-pyrid-2-ylamino}ethyl)-*N*-methylamino]pyrid-2-yl)aminomethylidenebisphosphonate;
- Tetraethyl *N*-(5-[3-{*N*-methyl-*N*-pyrid-2-ylamino}-1-oxoprop-1-yl]pyrid-2-yl)aminomethylidenebisphosphonate;
- 5 Tetraethyl *N*-(5-[2-{5-methyl-2-phenyloxazol-4-yl}ethoxy]pyrid-2-yl)aminomethylidenebisphosphonate
- Tetraethyl *N*-(5-[*N*-(2-{5-methyl-2-phenyloxazol-4-yl}ethyl)-*N*-methylamino]pyrid-2-yl)aminomethylidenebisphosphonate;
- Tetraethyl *N*-(5-[2-{5-methyl-2-phenylthiazol-4-yl}ethoxy]pyrid-2-yl)aminomethylidenebisphosphonate;
- 10 Tetraethyl *N*-(5-[3-{5-methyl-2-pyrid-4-yloxazol-4-yl}-1-oxoprop-1-yl]pyrid-2-yl)aminomethylidenebisphosphonate;
- Tetraethyl *N*-(5-[*N*-(2-{5-methyl-2-pyrid-4-ylthiazol-4-yl}ethyl)-*N*-methylamino]pyrid-2-yl)aminomethylidenebisphosphonate;
- 15 Tetraethyl *N*-(5-[2-{5-methyl-2-pyrid-4-yloxazol-4-yl}ethoxy]pyrid-2-yl)aminomethylidenebisphosphonate;
- Tetraethyl *N*-(5-[2-{5-methyl-2-pyrid-4-ylthiazol-4-yl}ethoxy]pyrid-2-yl)aminomethylidenebisphosphonate;
- 2-[1-Hydroxy-1-(5-[*N*-(2-{5-methyl-2-pyrid-4-ylthiazol-4-yl}ethyl)-*N*-methylamino]pyrid-2-yl)methyl]-1,3,2-dioxaphospholane-2-oxide;
- 20 2-[1-Hydroxy-1-(5-[2-{4-(4-trifluoromethylphenyl)phenoxy}ethoxy]-pyrid-2-yl)methyl]-1,3,2-dioxaphospholane-2-oxide;
- 2-[1-Hydroxy-1-(5-[*N*-(2-{4-(4-trifluoromethylphenyl)phenoxy}ethyl)-*N*-methylamino]pyrid-2-yl)methyl]-1,3,2-dioxaphospholane-2-oxide;

- 2-[1-Hydroxy-1-(5-[3-{4-(4-trifluoromethylphenyl)phenoxy}-1-oxoprop-1-yl]-pyrid-2-yl)methyl]-1,3,2-dioxaphospholane-2-oxide;
- 2-[1-Hydroxy-1-(5-[2-{1-[4-(2-trifluoromethylphenyl)phenylmethyl]-3-hexylureido}ethyl]pyrid-2-yl)methyl]-1,3,2-dioxaphospholane-2-oxide;
- 5 2-[1-Hydroxy-1-(5-[2-{1-butyl-3-(5-methoxypyrid-2-yl)ureido}ethyl]pyrid-2-ylmethyl)-1,3,2-dioxaphospholane-2-oxide;
- 2-[1-Hydroxy-1-(5-[3-{4-acetyl-3-hydroxy-2-propylphenoxy}propoxy]pyrid-2-ylmethyl)-1,3,2-dioxaphospholane-2-oxide;
- 2-[1-Hydroxy-1-(5-[2-{4*H*-3-oxobenzo[1,4]oxazin-2-yl}ethoxy]pyrid-2-yl)methyl]-1,3,2-dioxaphospholane-2-oxide;
- 10 2-[1-Hydroxy-1-(5-[3,*N*-phthalimidopropoxy]pyrid-2-yl)methyl]-1,3,2-dioxaphospholane-2-oxide;
- 2-[1-Hydroxy-1-(5-[4,*N*-phthalimidobutoxy]pyrid-2-yl)methyl]-1,3,2-dioxaphospholane-2-oxide;
- 15 2-[1-Hydroxy-1-(5-[2-{*N*-methyl-*N*-pyrid-2-ylamino}ethoxy]benzothien-2-yl)methyl]-[4*R*]-methyl-1,3,2-dioxaphospholane-2-oxide;
- 2-[1-Hydroxy-1-(5-[*N*-(2-{*N*-methyl-*N*-pyrid-2-ylamino}ethyl)-*N*-methylamino]benzothien-2-yl)methyl]-[4*R*]-methyl-1,3,2-dioxaphospholane-2-oxide;
- 2-[1-Hydroxy-1-(5-[3-{*N*-methyl-*N*-pyrid-2-ylamino}-1-oxoprop-1-yl]benzothien-2-yl)methyl]-[4*R*]-methyl-1,3,2-dioxaphospholane-2-oxide;
- 20 2-[1-Hydroxy-1-(5-[2-{5-methyl-2-phenyloxazol-4-yl}ethoxy]benzothien-2-yl)methyl]-[4*R*]-methyl-1,3,2-dioxaphospholane-2-oxide;
- 2-[1-Hydroxy-1-(5-[*N*-(2-{5-methyl-2-phenyloxazol-4-yl}ethyl)-*N*-methylamino]benzothien-2-yl)methyl]-[4*R*]-methyl-1,3,2-dioxaphospholane-2-oxide;

- 2-[1-Hydroxy-1-(5-[2-{5-methyl-2-phenylthiazol-4-yl}ethoxy]benzothien-2-yl)methyl]-  
[4R]-methyl-1,3,2-dioxaphospholane-2-oxide;
- 2-[1-Hydroxy-1-(5-[3-{5-methyl-2-phenylthiazol-4-yl}-1-oxoprop-1-yl]benzothien-2-  
yl)methyl]- [4R]-methyl-1,3,2-dioxaphospholane-2-oxide;
- 5 2-[1-Hydroxy-1-(5-[2-{5-methyl-2-pyrid-4-yloxazol-4-yl}ethoxy]benzothien-2-  
yl)methyl]- [4R]-methyl-1,3,2-dioxaphospholane-2-oxide;
- 2-[1-Hydroxy-1-(5-[2-{5-methyl-2-pyrid-4-ylthiazol-4-yl}ethoxy]benzothien-2-  
yl)methyl]- [4R]-methyl-1,3,2-dioxaphospholane-2-oxide;
- 2-[1-Hydroxy-1-(5-[3-{5-methyl-2-pyrid-4-yloxazol-4-yl}-1-oxoprop-1-yl]benzothien-2-  
10 yl)methyl]- [4R]-methyl-1,3,2-dioxaphospholane-2-oxide;
- 2-[1-Hydroxy-1-(5-[*N*-(2-{5-methyl-2-pyrid-4-ylthiazol-4-yl}ethyl)-*N*-  
methylamino]benzothien-2-yl)methyl]- [4S]-methyl-1,3,2-dioxaphospholane-2-oxide;
- 2-[1-Hydroxy-1-(5-[2-{4-(4-trifluoromethylphenyl)phenoxy}ethoxy]benzothien-2-  
yl)methyl]- [4S]-methyl-1,3,2-dioxaphospholane-2-oxide;
- 15 2-[1-Hydroxy-1-(5-[*N*-(2-{4-(4-trifluoromethylphenyl)phenoxy}ethyl)-*N*-  
methylamino]benzothien-2-yl)methyl]- [4S]-methyl-1,3,2-dioxaphospholane-2-oxide;
- 2-[1-Hydroxy-1-(5-[3-{4-(4-trifluoromethylphenyl)phenoxy}-1-oxoprop-1-yl]benzothien-  
2-yl)methyl]- [4S]-methyl-1,3,2-dioxaphospholane-2-oxide;
- 2-[1-Hydroxy-1-(5-[2-{1-[4-(2-trifluoromethylphenyl)phenylmethyl]-3-  
20 hexylureido}ethyl]benzothien-2-yl)methyl]- [4S]-methyl-1,3,2-dioxaphospholane-2-  
oxide;
- 2-[1-Hydroxy-1-(5-[2-{1-butyl-3-(5-methoxypyrid-2-yl)ureido}ethyl]benzothien-2-  
yl)methyl]- [4S]-methyl-1,3,2-dioxaphospholane-2-oxide;
- 2-[1-Hydroxy-1-(5-[3-{4-acetyl-3-hydroxy-2-propylphenoxy}propoxy]benzothien-2-  
25 yl)methyl]- [4S]-methyl-1,3,2-dioxaphospholane-2-oxide;



- 2-[1-Hydroxy-1-(5-[2-{4*H*-3-oxobenzo[1,4]oxazin-2-yl}ethoxy]benzothien-2-yl)methyl]-  
[4*S*]-methyl-1,3,2-dioxaphospholane-2-oxide;
- 2-[1-Hydroxy-1-(5-[3,*N*-phthalimidopropoxy]benzothien-2-yl)methyl]- [4*S*]-methyl-  
1,3,2-dioxaphospholane-2-oxide;
- 5 2-[1-Hydroxy-1-(5-[4,*N*-phthalimidobutoxy]benzothien-2-yl)methyl]- [4*S*]-methyl-1,3,2-  
dioxaphospholane-2-oxide;
- 2-[1-Hydroxy-1-(4-[2-{*N*-methyl-*N*-pyrid-2-ylamino}ethoxy]thiazol-2-yl)methyl]-4,5-  
dimethyl-1,3,2-dioxaphospholane-2-oxide;
- 2-[1-Hydroxy-1-(4-[*N*-(2-{*N*-methyl-*N*-pyrid-2-ylamino}ethyl)-*N*-methylamino]thiazol-2-  
10 yl)methyl]-4,5-dimethyl-1,3,2-dioxaphospholane-2-oxide;
- 2-[1-Hydroxy-1-(4-[3-{*N*-methyl-*N*-pyrid-2-ylamino}-1-oxoprop-1-yl]thiazol-2-  
yl)methyl]-4,5-dimethyl-1,3,2-dioxaphospholane-2-oxide;
- 2-[1-Hydroxy-1-(4-[2-{5-methyl-2-phenyloxazol-4-yl}ethoxy]thiazol-2-yl)methyl]-4,5-  
dimethyl-1,3,2-dioxaphospholane-2-oxide;
- 15 2-[1-Hydroxy-1-(4-[*N*-(2-{5-methyl-2-phenyloxazol-4-yl}ethyl)-*N*-methylamino]thiazol-  
2-yl)methyl]-4,5-dimethyl-1,3,2-dioxaphospholane-2-oxide;
- 2-[1-Hydroxy-1-(4-[2-{5-methyl-2-phenylthiazol-4-yl}ethoxy]thiazol-2-yl)methyl]-4,5-  
dimethyl-1,3,2-dioxaphospholane-2-oxide;
- 2-[1-Hydroxy-1-(4-[3-{5-methyl-2-phenylthiazol-4-yl}-1-oxoprop-1-yl]thiazol-2-  
20 yl)methyl]-4,5-dimethyl-1,3,2-dioxaphospholane-2-oxide;
- 2-[1-Hydroxy-1-(4-[2-{5-methyl-2-pyrid-4-ylloxazol-4-yl}ethoxy]thiazol-2-yl)methyl]-  
4,5-dimethyl-1,3,2-dioxaphospholane-2-oxide;
- 2-[1-Hydroxy-1-(4-[2-{5-methyl-2-pyrid-4-ylthiazol-4-yl}ethoxy]thiazol-2-yl)methyl]-  
4,5-dimethyl-1,3,2-dioxaphospholane-2-oxide;

- 2-[1-Hydroxy-1-(4-[3-{5-methyl-2-pyrid-4-yloxazol-4-yl}-1-oxoprop-1-yl]thiazol-2-yl)methyl]-4,5-dimethyl-1,3,2-dioxaphospholane-2-oxide;
- 2-[1-Hydroxy-1-(4-[*N*-(2-{5-methyl-2-pyrid-4-ylthiazol-4-yl}ethyl)-*N*-methylamino]thiazol-2-yl)methyl]-1,3,2-dioxaphosphinane-2-oxide;
- 5 2-[1-Hydroxy-1-(4-[2-{4-(4-trifluoromethylphenyl)phenoxy}ethoxy]thiazol-2-yl)methyl]-1,3,2-dioxaphosphinane-2-oxide;
- 2-[1-Hydroxy-1-(4-[*N*-(2-{4-(4-trifluoromethylphenyl)phenoxy}ethyl)-*N*-methylamino]thiazol-2-yl)methyl]-1,3,2-dioxaphosphinane-2-oxide;
- 2-[1-Hydroxy-1-(4-[3-{4-(4-trifluoromethylphenyl)phenoxy}-1-oxoprop-1-yl]thiazol-2-yl)methyl]-1,3,2-dioxaphosphinane-2-oxide;
- 10 2-[1-Hydroxy-1-(4-[2-{1-[4-(2-trifluoromethylphenyl)phenylmethyl]-3-hexylureido}ethyl]thiazol-2-yl)methyl]-1,3,2-dioxaphosphinane-2-oxide;
- 2-[1-Hydroxy-1-(4-[2-{1-butyl-3-(5-methoxypyrid-2-yl)ureido}ethyl]thiazol-2-yl)methyl]-1,3,2-dioxaphosphinane-2-oxide;
- 15 2-[1-Hydroxy-1-(4-[3-{4-acetyl-3-hydroxy-2-propylphenoxy}propoxy]thiazol-2-yl)methyl]-1,3,2-dioxaphosphinane-2-oxide;
- 2-[1-Hydroxy-1-(4-[2-{4*H*-3-oxobenzo[1,4]oxazin-2-yl}ethoxy]thiazol-2-yl)methyl]-1,3,2-dioxaphosphinane-2-oxide;
- 2-[1-Hydroxy-1-(4-[3,*N*-phthalimidopropoxy]thiazol-2-yl)methyl]-1,3,2-dioxaphosphinane-2-oxide;
- 20 2-[1-Hydroxy-1-(4-[4,*N*-phthalimidobutoxy]thiazol-2-yl)methyl]-1,3,2-dioxaphosphinane-2-oxide;
- 2[1-(6-[2-{*N*-methyl-*N*-pyrid-2-ylamino}ethoxy]-3-methoxyquinolin-2-yl)-1-(2-oxido-1,3,2-dioxaphospholan-2-yl)methoxy]-1,3,2-dioxaphospholane-2-oxide;

- 2[1-(6-[*N*-(2-{*N*-methyl-*N*-pyrid-2-ylamino}ethyl)-*N*-methylamino]-3-methoxyquinolin-2-yl)-1-(2-oxido-1,3,2-dioxaphospholan-2-yl)methoxy]-1,3,2-dioxaphospholane-2-oxide;
- 2[1-(6-[3-{*N*-methyl-*N*-pyrid-2-ylamino}-1-oxoprop-1-yl]-3-methoxyquinolin-2-yl)-1-(2-oxido-1,3,2-dioxaphospholan-2-yl)methoxy]-1,3,2-dioxaphospholane-2-oxide;
- 2[1-(6-[2-{5-methyl-2-phenyloxazol-4-yl}ethoxy]-3-methoxyquinolin-2-yl)-1-(2-oxido-1,3,2-dioxaphospholan-2-yl)methoxy]-1,3,2-dioxaphospholane-2-oxide;
- 2[1-(6-[*N*-(2-{5-methyl-2-phenyloxazol-4-yl}ethyl)-*N*-methylamino]-3-methoxyquinolin-2-yl)-1-(2-oxido-1,3,2-dioxaphospholan-2-yl)methoxy]-1,3,2-dioxaphospholane-2-oxide;
- 2[1-(6-[2-{5-methyl-2-phenylthiazol-4-yl}ethoxy]-3-methoxyquinolin-2-yl)-1-(2-oxido-1,3,2-dioxaphospholan-2-yl)methoxy]-1,3,2-dioxaphospholane-2-oxide;
- 2[1-(6-[3-{5-methyl-2-phenylthiazol-4-yl}-1-oxoprop-1-yl]-3-methoxyquinolin-2-yl)-1-(2-oxido-1,3,2-dioxaphospholan-2-yl)methoxy]-1,3,2-dioxaphospholane-2-oxide;
- 2[1-(6-[2-{5-methyl-2-pyrid-4-yloxazol-4-yl}ethoxy]-3-methoxyquinolin-2-yl)-1-(2-oxido-1,3,2-dioxaphospholan-2-yl)methoxy]-1,3,2-dioxaphospholane-2-oxide;
- 2[1-(6-[2-{5-methyl-2-pyrid-4-ylthiazol-4-yl}ethoxy]-3-methoxyquinolin-2-yl)-1-(2-oxido-1,3,2-dioxaphospholan-2-yl)methoxy]-1,3,2-dioxaphospholane-2-oxide;
- 2[1-(6-[3-{5-methyl-2-pyrid-4-yloxazol-4-yl}-1-oxoprop-1-yl]-3-methoxyquinolin-2-yl)-1-(2-oxido-1,3,2-dioxaphospholan-2-yl)methoxy]-1,3,2-dioxaphospholane-2-oxide;
- 2[1-(6-[*N*-(2-{5-methyl-2-pyrid-4-ylthiazol-4-yl}ethyl)-*N*-methylamino]-3-methoxyquinolin-2-yl)-1-([4*R*]-methyl-2-oxido-1,3,2-dioxaphospholan-2-yl)methoxy]-[4*R*]-methyl-1,3,2-dioxaphospholane-2-oxide;

- 2[1-(6-[2-{4-(4-trifluoromethylphenyl)phenoxy}ethoxy]-3-methoxyquinolin-2-yl)-1-  
([4R]-methyl-2-oxido-1,3,2-dioxaphospholan-2-yl)methoxy]-[4R]-methyl-1,3,2-  
dioxaphospholane-2-oxide;
- 2[1-(6-[*N*-(2-{4-(4-trifluoromethylphenyl)phenoxy}ethyl)-*N*-methylamino]-3-  
5 methoxyquinolin-2-yl)-1-([4R]-methyl-2-oxido-1,3,2-dioxaphospholan-2-  
yl)methoxy]-[4R]-methyl-1,3,2-dioxaphospholane-2-oxide;
- 2[1-(6-[3-{4-(4-trifluoromethylphenyl)phenoxy}-1-oxoprop-1-yl]-3-methoxyquinolin-2-  
yl)-1-([4R]-methyl-2-oxido-1,3,2-dioxaphospholan-2-yl)methoxy]-[4R]-methyl-1,3,2-  
dioxaphospholane-2-oxide;
- 10 2[1-(6-[2-{1-[4-(2-trifluoromethylphenyl)phenylmethyl]-3-hexylureido}ethyl]-3-  
methoxyquinolin-2-yl)-1-([4R]-methyl-2-oxido-1,3,2-dioxaphospholan-2-  
yl)methoxy]-[4R]-methyl-1,3,2-dioxaphospholane-2-oxide;
- 2[1-(6-[2-{1-butyl-3-(5-methoxypyrid-2-yl)ureido}ethyl]-3-methoxyquinolin-2-yl)-1-  
([4R]-methyl-2-oxido-1,3,2-dioxaphospholan-2-yl)methoxy]-[4R]-methyl-1,3,2-  
15 dioxaphospholane-2-oxide;
- 2[1-(6-[3-{4-acetyl-3-hydroxy-2-propylphenoxy}propoxy]-3-methoxyquinolin-2-yl)-1-  
([4R]-methyl-2-oxido-1,3,2-dioxaphospholan-2-yl)methoxy]-[4R]-methyl-1,3,2-  
dioxaphospholane-2-oxide;
- 2[1-(6-[2-{4*H*-3-oxobenzo[1,4]oxazin-2-yl}ethoxy]-3-methoxyquinolin-2-yl)-1-([4R]-  
20 methyl-2-oxido-1,3,2-dioxaphospholan-2-yl)methoxy]-[4R]-methyl-1,3,2-  
dioxaphospholane-2-oxide;
- 2[1-(6-[3,*N*-phthalimidopropoxy]-3-methoxyquinolin-2-yl)-1-([4R]-methyl-2-oxido-1,3,2-  
dioxaphospholan-2-yl)methoxy]-[4R]-methyl-1,3,2-dioxaphospholane-2-oxide;
- 2[1-(6-[4,*N*-phthalimidobutoxy]-3-methoxyquinolin-2-yl)-1-([4R]-methyl-2-oxido-1,3,2-  
25 dioxaphospholan-2-yl)methoxy]-[4R]-methyl-1,3,2-dioxaphospholane-2-oxide;

- 2[1-(5-[2-{*N*-methyl-*N*-pyrid-2-ylamino}ethoxy]thien-2-yl)-1-([4*S*]-methyl-2-oxido-  
1,3,2-dioxaphospholan-2-yl)methoxy]- [4*S*]-methyl-1,3,2-dioxaphospholane-2-oxide;
- 2[1-(5-[*N*-(2-{*N*-methyl-*N*-pyrid-2-ylamino}ethyl)-*N*-methylamino]thien-2-yl)-1-([4*S*]-  
methyl-2-oxido-1,3,2-dioxaphospholan-2-yl)methoxy]- [4*S*]-methyl-1,3,2-  
5 dioxaphospholane-2-oxide;
- 2[1-(5-[3-{*N*-methyl-*N*-pyrid-2-ylamino}-1-oxoprop-1-yl]thien-2-yl)-1-([4*S*]-methyl-2-  
oxido-1,3,2-dioxaphospholan-2-yl)methoxy]- [4*S*]-methyl-1,3,2-dioxaphospholane-2-  
oxide;
- 2[1-(5-[2-{5-methyl-2-phenyloxazol-4-yl}ethoxy]thien-2-yl)-1-([4*S*]-methyl-2-oxido-  
10 1,3,2-dioxaphospholan-2-yl)methoxy]- [4*S*]-methyl-1,3,2-dioxaphospholane-2-oxide;
- 2[1-(5-[*N*-(2-{5-methyl-2-phenyloxazol-4-yl}ethyl)-*N*-methylamino]thien-2-yl)-1-([4*S*]-  
methyl-2-oxido-1,3,2-dioxaphospholan-2-yl)methoxy]- [4*S*]-methyl-1,3,2-  
dioxaphospholane-2-oxide;
- 2[1-(5-[2-{5-methyl-2-phenylthiazol-4-yl}ethoxy]thien-2-yl)-1-([4*S*]-methyl-2-oxido-  
15 1,3,2-dioxaphospholan-2-yl)methoxy]- [4*S*]-methyl-1,3,2-dioxaphospholane-2-oxide;
- 2[1-(5-[3-{5-methyl-2-phenylthiazol-4-yl}-1-oxoprop-1-yl]thien-2-yl)-1-([4*S*]-methyl-2-  
oxido-1,3,2-dioxaphospholan-2-yl)methoxy]- [4*S*]-methyl-1,3,2-dioxaphospholane-2-  
oxide;
- 2[1-(5-[2-{5-methyl-2-pyrid-4-yloxazol-4-yl}ethoxy]thien-2-yl)-1-([4*S*]-methyl-2-oxido-  
20 1,3,2-dioxaphospholan-2-yl)methoxy]- [4*S*]-methyl-1,3,2-dioxaphospholane-2-oxide;
- 2[1-(5-[2-{5-methyl-2-pyrid-4-ylthiazol-4-yl}ethoxy]thien-2-yl)-1-([4*S*]-methyl-2-oxido-  
1,3,2-dioxaphospholan-2-yl)methoxy]- [4*S*]-methyl-1,3,2-dioxaphospholane-2-oxide;
- 2[1-(5-[3-{5-methyl-2-pyrid-4-yloxazol-4-yl}-1-oxoprop-1-yl]thien-2-yl)-1-([4*S*]-methyl-  
2-oxido-1,3,2-dioxaphospholan-2-yl)methoxy]- [4*S*]-methyl-1,3,2-dioxaphospholane-  
25 2-oxide;

2[1-(5-[*N*-(2-{5-methyl-2-pyrid-4-ylthiazol-4-yl}ethyl)-*N*-methylamino]thien-2-yl)-1-

(4,5-dimethyl-2-oxido-1,3,2-dioxaphospholan-2-yl)methoxy]-4,5-dimethyl-1,3,2-dioxaphospholane-2-oxide;

2[1-(5-[2-{4-(4-trifluoromethylphenyl)phenoxy}ethoxy]thien-2-yl)-1-(4,5-dimethyl-2-

5 oxido-1,3,2-dioxaphospholan-2-yl)methoxy]-4,5-dimethyl-1,3,2-dioxaphospholane-2-oxide;

2[1-(5-[*N*-(2-{4-(4-trifluoromethylphenyl)phenoxy}ethyl)-*N*-methylamino]thien-2-yl)-1-

(4,5-dimethyl-2-oxido-1,3,2-dioxaphospholan-2-yl)methoxy]-4,5-dimethyl-1,3,2-dioxaphospholane-2-oxide;

10 2[1-(5-[3-{4-(4-trifluoromethylphenyl)phenoxy}-1-oxoprop-1-yl]thien-2-yl)-1-(4,5-dimethyl-2-oxido-1,3,2-dioxaphospholan-2-yl)methoxy]-4,5-dimethyl-1,3,2-dioxaphospholane-2-oxide;

2[1-(5-[2-{1-[4-(2-trifluoromethylphenyl)phenylmethyl]-3-hexylureido}ethyl]thien-2-yl)-

1-(4,5-dimethyl-2-oxido-1,3,2-dioxaphospholan-2-yl)methoxy]-4,5-dimethyl-1,3,2-

15 dioxaphospholane-2-oxide;

2[1-(5-[2-{1-butyl-3-(5-methoxypyrid-2-yl)ureido}ethyl]thien-2-yl)-1-(4,5-dimethyl-2-

oxido-1,3,2-dioxaphospholan-2-yl)methoxy]-4,5-dimethyl-1,3,2-dioxaphospholane-2-oxide;

2[1-(5-[3-{4-acetyl-3-hydroxy-2-propylphenoxy}propoxy]thien-2-yl)-1-(4,5-dimethyl-2-

20 oxido-1,3,2-dioxaphospholan-2-yl)methoxy]-4,5-dimethyl-1,3,2-dioxaphospholane-2-oxide;

2[1-(5-[2-{4*H*-3-oxobenzo[1,4]oxazin-2-yl}ethoxy]thien-2-yl)-1-(4,5-dimethyl-2-oxido-

1,3,2-dioxaphospholan-2-yl)methoxy]-4,5-dimethyl-1,3,2-dioxaphospholane-2-oxide;

2[1-(5-[3,*N*-phthalimidopropoxy]thien-2-yl)-1-(4,5-dimethyl-2-oxido-1,3,2-

25 dioxaphospholan-2-yl)methoxy]-4,5-dimethyl-1,3,2-dioxaphospholane-2-oxide;

- 2[1-(5-[4,*N*-phthalimidobutoxy]thien-2-yl)-1-(4,5-dimethyl-2-oxido-1,3,2-dioxaphospholan-2-yl)methoxy]-4,5-dimethyl-1,3,2-dioxaphospholane-2-oxide;
- 2[1-(4-[2-{*N*-methyl-*N*-pyrid-2-ylamino}ethoxy]-3-fluorophenyl)-1-(2-oxido-1,3,2-dioxaphosphinan-2-yl)methoxy]-1,3,2-dioxaphosphinane-2-oxide;
- 5 2[1-(4-[*N*-(2-{*N*-methyl-*N*-pyrid-2-ylamino}ethyl)-*N*-methylaminocarbonyl]-3-fluorophenyl)-1-(2-oxido-1,3,2-dioxaphosphinan-2-yl)methoxy]-1,3,2-dioxaphosphinane-2-oxide;
- 2[1-(4-[3-{*N*-methyl-*N*-pyrid-2-ylamino}-1-oxoprop-1-yl]-3-fluorophenyl)-1-(2-oxido-1,3,2-dioxaphosphinan-2-yl)methoxy]-1,3,2-dioxaphosphinane-2-oxide;
- 10 2[1-(4-[2-{5-methyl-2-phenyloxazol-4-yl}ethoxy]-3-fluorophenyl)-1-(2-oxido-1,3,2-dioxaphosphinan-2-yl)methoxy]-1,3,2-dioxaphosphinane-2-oxide;
- 1-(4-[*N*-(2-{5-methyl-2-phenyloxazol-4-yl}ethyl)-*N*-methylaminocarbonyl]-3-fluorophenyl)-1,1-bis(2-oxido-1,3,2-dioxaphospholan-2-yl)methane;
- 1-(4-[2-{5-methyl-2-phenylthiazol-4-yl}ethoxy]-3-fluorophenyl)-1,1-bis(2-oxido-1,3,2-dioxaphospholan-2-yl)methane;
- 15 1-(4-[3-{5-methyl-2-phenylthiazol-4-yl}-1-oxoprop-1-yl]-3-fluorophenyl)-1,1-bis(2-oxido-1,3,2-dioxaphospholan-2-yl)methane;
- 1-(4-[2-{5-methyl-2-pyrid-4-ylloxazol-4-yl}ethoxy]-3-fluorophenyl)-1,1-bis(2-oxido-1,3,2-dioxaphospholan-2-yl)methane;
- 20 1-(4-[2-{5-methyl-2-pyrid-4-ylthiazol-4-yl}ethoxy]-3-fluorophenyl)-1,1-bis(4,5-dimethyl-2-oxido-1,3,2-dioxaphospholan-2-yl)methane;
- 1-(4-[3-{5-methyl-2-pyrid-4-ylloxazol-4-yl}-1-oxoprop-1-yl]-3-fluorophenyl)-1,1-bis(2-oxido-1,3,2-dioxaphosphinan-2-yl)methane;
- 1-(4-[*N*-(2-{5-methyl-2-pyrid-4-ylthiazol-4-yl}ethyl)-*N*-methylaminocarbonyl]-3-fluorophenyl)-1,1-bis(4,5-dimethyl-2-oxido-1,3,2-dioxaphospholan-2-yl)methane;
- 25

- 1-(4-[2-{4-(4-trifluoromethylphenyl)phenoxy}ethoxy]-3-fluorophenyl)-1,1-bis(2-oxido-1,3,2-dioxaphosphinan-2-yl)methane;
- 1-(4-[*N*-(2-{4-(4-trifluoromethylphenyl)phenoxy}ethyl)-*N*-methylaminocarbonyl]-3-fluorophenyl)-1,1-bis(4,5-dimethyl-2-oxido-1,3,2-dioxaphospholan-2-yl)methane;
- 5 1-(4-[3-{4-(4-trifluoromethylphenyl)phenoxy}-1-oxoprop-1-yl]-3-fluorophenyl)-1,1-bis(2-oxido-1,3,2-dioxaphosphinan-2-yl)methane;
- 1-(4-[2-{1-[4-(2-trifluoromethylphenyl)phenylmethyl]-3-hexylureido}ethyl]-3-fluorophenyl)-1,1-bis(4,5-dimethyl-2-oxido-1,3,2-dioxaphospholan-2-yl)methane;
- 1-(4-[2-{1-butyl-3-(5-methoxypyrid-2-yl)ureido}ethyl]-3-fluorophenyl)-1,1-bis(2-oxido-1,3,2-dioxaphosphinan-2-yl)methane;
- 10 2-(4-[3-{4-acetyl-3-hydroxy-2-propylphenoxy}propoxy]-3-fluorophenyl)-1,2-bis(2-oxido-1,3,2-dioxaphospholan-2-yl)ethane;
- 2-(4-[2-{4*H*-3-oxobenzo[1,4]oxazin-2-yl}ethoxy]-3-fluorophenyl)-1,2-bis([4*R*]-methyl-2-oxido-1,3,2-dioxaphospholan-2-yl)ethane;
- 15 2-(4-[3,*N*-phthalimidopropoxy]-3-fluorophenyl)-1,2-bis(2-oxido-1,3,2-dioxaphospholan-2-yl)ethane;
- 2-(4-[4,*N*-phthalimidobutoxy]-3-fluorophenyl)-1,2-bis([4*R*]-methyl-2-oxido-1,3,2-dioxaphospholan-2-yl)ethane;
- 2-(3-[3-{*N*-methyl-*N*-pyrid-2-ylamino}propoxy]-4-fluorophenyl)-1,2-bis(2-oxido-1,3,2-dioxaphospholan-2-yl)ethane;
- 20 2-(3-[*N*-(3-{*N*-methyl-*N*-pyrid-2-ylamino}propyl)-*N*-methylamino]-4-fluorophenyl)-1,2-bis([4*R*]-methyl-2-oxido-1,3,2-dioxaphospholan-2-yl)ethane;
- 2-(3-[3-{*N*-methyl-*N*-pyrid-2-ylamino}-1-oxoprop-1-ylamino]-4-fluorophenyl)-1,2-bis(2-oxido-1,3,2-dioxaphospholan-2-yl)ethane;



- 2-(3-[3-{5-methyl-2-phenyloxazol-4-yl}propoxy]-4-fluorophenyl)-1,2-bis([4R]-methyl-2-oxido-1,3,2-dioxaphospholan-2-yl)ethane;
- 2-(3-[N-(2-{5-methyl-2-phenyloxazol-4-yl}ethyl)-N-methylaminocarbonyl]-4-methoxyphenyl)-1,1-bis(4,5-dimethyl-2-oxido-1,3,2-dioxaphospholan-2-yl)ethane;
- 5 2-(3-[3-{5-methyl-2-phenylthiazol-4-yl}propoxy]-4-fluorophenyl)-1,1-bis(2-oxido-1,3,2-dioxaphosphinan-2-yl)ethane;
- 2-(3-[3-{5-methyl-2-phenylthiazol-4-yl}-1-oxoprop-1-yl]-4-fluorophenyl)-1,1-bis(4,5-dimethyl-2-oxido-1,3,2-dioxaphospholan-2-yl)ethane;
- 2-(3-[4-{5-methyl-2-pyrid-4-yloxazol-4-yl}butoxy]-4-fluorophenyl)-1,1-bis(2-oxido-1,3,2-dioxaphosphinan-2-yl)ethane;
- 10 1,3,2-dioxaphosphinan-2-yl)ethane;
- 2-(3-[3-{5-methyl-2-pyrid-4-ylthiazol-4-yl}propoxy]-4-fluorophenyl)-1,1-bis(4,5-dimethyl-2-oxido-1,3,2-dioxaphospholan-2-yl)ethane;
- 2-(3-[3-{5-methyl-2-pyrid-4-yloxazol-4-yl}-1-oxoprop-1-ylthio]-4-fluorophenyl)-1,1-bis(2-oxido-1,3,2-dioxaphosphinan-2-yl)ethane;
- 15 2-(3-[N-(3-{5-methyl-2-pyrid-4-ylthiazol-4-yl}propyl)-N-methylamino]-4-fluorophenyl)-1,1-bis(4,5-dimethyl-2-oxido-1,3,2-dioxaphospholan-2-yl)ethane;
- 2-(3-[3-{4-(4-trifluoromethylphenyl)phenoxy}propoxy]-4-fluorophenyl)-1,1-bis(2-oxido-1,3,2-dioxaphosphinan-2-yl)ethane;
- 1-[N-(3-[N-(3-{4-(4-trifluoromethylphenyl)phenoxy}propyl)-N-methylamino]-4-fluorophenyl)amino]-1,1-bis(2-oxido-1,3,2-dioxaphospholan-2-yl)methane;
- 20 1-[N-(3-[4-{4-(4-trifluoromethylphenyl)phenoxy}-1-oxobut-1-yl]-4-fluorophenyl)amino]-1,1-bis([4R]-methyl-2-oxido-1,3,2-dioxaphospholan-2-yl)methane;
- 1-[N-(3-[2-{1-[4-(2-trifluoromethylphenyl)phenylmethyl]-3-hexylureido}ethyl]-4-fluorophenyl)amino]-1,1-bis(2-oxido-1,3,2-dioxaphospholan-2-yl)methane;

- 1-[*N*-(3-[2-{1-butyl-3-(5-methoxypyrid-2-yl)ureido}ethyl]-4-fluorophenyl)amino]-1,1-bis([4*R*]-methyl-2-oxido-1,3,2-dioxaphospholan-2-yl)methane;
- 1-[*N*-(3-[4-{4-acetyl-3-hydroxy-2-propylphenoxy}butoxy]-4-fluorophenyl)amino]-1,1-bis(2-oxido-1,3,2-dioxaphospholan-2-yl)methane;
- 5 1-[*N*-(3-[3-{4*H*-3-oxobenzo[1,4]oxazin-2-yl}propoxy]-4-fluorophenyl)amino]-1,1-bis([4*R*]-methyl-2-oxido-1,3,2-dioxaphospholan-2-yl)methane;
- 1-[*N*-(3-[3,*N*-phthalimidopropoxy]-4-fluorophenyl)amino]-1,1-bis(2-oxido-1,3,2-dioxaphospholan-2-yl)methane;
- 1-[*N*-(3-[4,*N*-phthalimidobutoxy]-4-fluorophenyl)amino]-1,1-bis([4*R*]-methyl-2-oxido-1,3,2-dioxaphospholan-2-yl)methane;
- 10 1-[*N*-(6-[2-{*N*-methyl-*N*-pyrid-2-ylamino}ethoxy]indol-2-yl)amino]-1,1-bis(2-oxido-1,3,2-dioxaphosphinan-2-yl)methane;
- 1-[*N*-(6-[*N*-(2-{*N*-methyl-*N*-pyrid-2-ylamino}ethyl)-*N*-methylamino]indol-2-yl)amino]-1,1-bis(2-oxido-1,3,2-dioxaphosphinan-2-yl)methane;
- 15 1-[*N*-(6-[3-{*N*-methyl-*N*-pyrid-2-ylamino}-1-oxoprop-1-yl]indol-2-yl)amino]-1,1-bis(2-oxido-1,3,2-dioxaphosphinan-2-yl)methane;
- 1-[*N*-(6-[2-{5-methyl-2-phenyloxazol-4-yl}ethoxy] indol-2-yl)amino]-1,1-bis(2-oxido-1,3,2-dioxaphosphinan-2-yl)methane;
- 2-[1-(Diethoxyphosphinyloxy)-1-(6-[*N*-(2-{5-methyl-2-phenyloxazol-4-yl}ethyl)-*N*-methylamino] indol-2-yl)methyl]-1,3,2-dioxaphospholane-2-oxide;
- 20 2-[1-(Diethoxyphosphinyloxy)-1-(6-[2-{5-methyl-2-phenylthiazol-4-yl}ethoxy]indol-2-yl)methyl]-1,3,2-dioxaphospholane-2-oxide;
- 2-[1-(Diethoxyphosphinyloxy)-1-(6-[3-{5-methyl-2-phenylthiazol-4-yl}-1-oxoprop-1-yl]indol-2-yl)methyl]-1,3,2-dioxaphospholane-2-oxide;

- 2-[1-(Diethoxyphosphinyloxy)-1-(6-[2-{5-methyl-2-pyrid-4-yloxazol-4-yl} ethoxy]indol-2-yl)methyl]-1,3,2-dioxaphospholane-2-oxide;
- 2-[1-(Diethoxyphosphinyloxy)-1-(6-[2-{5-methyl-2-pyrid-4-ylthiazol-4-yl} ethoxy]indol-2-yl)methyl]-1,3,2-dioxaphosphinane-2-oxide;
- 5 2-[1-(Diethoxyphosphinyloxy)-1-(6-[3-{5-methyl-2-pyrid-4-yloxazol-4-yl}-1-oxoprop-1-yl]indol-2-yl)methyl]-1,3,2-dioxaphosphinane-2-oxide;
- 2-[1-(Diethoxyphosphinyloxy)-1-(6-[*N*-(2-{5-methyl-2-pyrid-4-ylthiazol-4-yl} ethyl)-*N*-methylamino]indol-2-yl)methyl]-1,3,2-dioxaphosphinane-2-oxide;
- 2-[1-(Diethoxyphosphinyloxy)-1-(6-[2-{4-(4-trifluoromethylphenyl)phenoxy} ethoxy]
- 10 indol-2-yl)methyl]-1,3,2-dioxaphosphinane-2-oxide;
- 2[1-(6-[*N*-(2-{4-(4-trifluoromethylphenyl)phenoxy} ethyl)-*N*-methylamino]indol-2-yl)-1-(diethoxyphosphinyl)methoxy]-4[*S*]-methyl-1,3,2-dioxaphospholane-2-oxide;
- 2[1-(6-[3-{4-(4-trifluoromethylphenyl)phenoxy}-1-oxoprop-1-yl]indol-2-yl)-1-(diethoxyphosphinyl)methoxy]-4,5-dimethyl-1,3,2-dioxaphospholane-2-oxide;
- 15 2[1-(6-[2-{1-[4-(2-trifluoromethylphenyl)phenylmethyl]-3-hexylureido} ethyl]indol-2-yl)-1-(diethoxyphosphinyl)methoxy]-4[*S*]-methyl-1,3,2-dioxaphospholane-2-oxide;
- 2[1-(6-[2-{1-[4-(2-trifluoromethylphenyl)phenylmethyl]-3-hexylureido} ethyl]indol-2-yl)-1-(diethoxyphosphinyl)methoxy]-4,5-dimethyl-1,3,2-dioxaphospholane-2-oxide;
- 2[1-(6-[3-{4-acetyl-3-hydroxy-2-propylphenoxy}propoxy]indol-2-yl)-1-
- 20 (diethoxyphosphinyl)methoxy]-4[*S*]-methyl-1,3,2-dioxaphospholane-2-oxide;
- 2[1-(6-[2-{4*H*-3-oxobenzo[1,4]oxazin-2-yl} ethoxy]indol-2-yl)-1-(diethoxyphosphinyl)methoxy]-4,5-dimethyl-1,3,2-dioxaphospholane-2-oxide;
- 2[1-(6-[2-{1-butyl-3-(5-methoxypyrid-2-yl)ureido} ethyl]indol-2-yl)-1-(diethoxyphosphinyl)methoxy]-4[*S*]-methyl-1,3,2-dioxaphospholane-2-oxide;

- 2[1-(6-[3,*N*-phthalimidopropoxy]indol-2-yl)-1-(diethoxyphosphinyl)methoxy]-4,5-dimethyl-1,3,2-dioxaphospholane-2-oxide;
- 2[1-(6-[4,*N*-phthalimidobutoxy]indol-2-yl)-1-(diethoxyphosphinyl)methyl]-4[R]-methyl-1,3,2-dioxaphospholane-2-oxide;
- 5 2[1-(5-[2-{*N*-methyl-*N*-pyrid-2-ylamino}ethoxy]pyrid-2-yl)-1-(diethoxyphosphinyl)methyl]-4[R]-methyl-1,3,2-dioxaphospholane-2-oxide;
- 2[1-(5-[*N*-(2-{*N*-methyl-*N*-pyrid-2-ylamino}ethyl)-*N*-methylamino]pyrid-2-yl)-1-(diethoxyphosphinyl)methyl]-4[R]-methyl-1,3,2-dioxaphospholane-2-oxide;
- 2[1-(5-[3-{*N*-methyl-*N*-pyrid-2-ylamino}-1-oxoprop-1-yl]pyrid-2-yl)-1-(diethoxyphosphinyl)methyl]-4[R]-methyl-1,3,2-dioxaphospholane-2-oxide;
- 10 2[1-(5-[2-{5-methyl-2-phenyloxazol-4-yl}ethoxy]pyrid-2-yl)-1-(diethoxyphosphinyl)methyl]-1,3,2-dioxaphosphinane-2-oxide;
- 2[1-(5-[*N*-(2-{5-methyl-2-phenyloxazol-4-yl}ethyl)-*N*-methylamino]pyrid-2-yl)-1-(diethoxyphosphinyl)methyl]-1,3,2-dioxaphosphinane-2-oxide;
- 15 2[1-(5-[*N*-(2-{5-methyl-2-phenyloxazol-4-yl}ethyl)-*N*-methylamino]pyrid-2-yl)-1-(diethoxyphosphinyl)methyl]-1,3,2-dioxaphosphinane-2-oxide;
- 2[1-(5-[2-{5-methyl-2-phenylthiazol-4-yl}ethoxy]pyrid-2-yl)-1-(diethoxyphosphinyl)methyl]-1,3,2-dioxaphosphinane-2-oxide;
- 2[1-(5-[3-{5-methyl-2-phenylthiazol-4-yl}-1-oxoprop-1-yl]pyrid-2-yl)-2-(diethoxyphosphinyl)eth-1-yl]-4,5-dimethyl-1,3,2-dioxaphospholane-2-oxide;
- 20 2[1-(5-[2-{5-methyl-2-pyrid-4-ylloxazol-4-yl}ethoxy]pyrid-2-yl)-2-(diethoxyphosphinyl)eth-1-yl]-1,3,2-dioxaphosphinane-2-oxide;
- 2[1-(5-[2-{5-methyl-2-pyrid-4-ylthiazol-4-yl}ethoxy]pyrid-2-yl)-2-(diethoxyphosphinyl)eth-1-yl]-4,5-dimethyl-1,3,2-dioxaphospholane-2-oxide;

- 2[1-(5-[3-{5-methyl-2-pyrid-4-yloxazol-4-yl}-1-oxoprop-1-yl]pyrid-2-yl)-2-(diethoxyphosphinyl)eth-1-yl]-1,3,2-dioxaphosphinane-2-oxide;
- 2[1-(5-[*N*-(2-{5-methyl-2-pyrid-4-ylthiazol-4-yl}ethyl)-*N*-methylamino]pyrid-2-yl)-2-(diethoxyphosphinyl)eth-1-yl]-4,5-dimethyl-1,3,2-dioxaphospholane-2-oxide;
- 5 2[1-(5-[2-{4-(4-trifluoromethylphenyl)phenoxy}ethoxy]-pyrid-2-yl)-2-(diethoxyphosphinyl)eth-1-yl]-1,3,2-dioxaphosphinane-2-oxide;
- 2[1-(5-[*N*-(2-{4-(4-trifluoromethylphenyl)phenoxy}ethyl)-*N*-methylamino]pyrid-2-yl)-2-(diethoxyphosphinyl)eth-1-yl]-4,5-dimethyl-1,3,2-dioxaphospholane-2-oxide;
- 2[1-(5-[3-{4-(4-trifluoromethylphenyl)phenoxy}-1-oxoprop-1-yl]-pyrid-2-yl)-2-(diethoxyphosphinyl)eth-1-yl]-1,3,2-dioxaphosphinane-2-oxide;
- 10 2[2-(5-[2-{1-[4-(2-trifluoromethylphenyl)phenylmethyl]-3-hexylureido}ethyl]pyrid-2-yl)-2-(diethoxyphosphinyl)eth-1-yl]-1,3,2-dioxaphospholane-2-oxide;
- 2[2-(5-[2-{1-butyl-3-(5-methoxypyrid-2-yl)ureido}ethyl]pyrid-2-yl)-2-(diethoxyphosphinyl)eth-1-yl]-4[R]-methyl-1,3,2-dioxaphospholane-2-oxide;
- 15 2[2-(5-[3-{4-acetyl-3-hydroxy-2-propylphenoxy}propoxy]pyrid-2-yl)-2-(diethoxyphosphinyl)eth-1-yl]-1,3,2-dioxaphospholane-2-oxide;
- 2[2-(5-[2-{4*H*-3-oxobenzo[1,4]oxazin-2-yl}ethoxy]pyrid-2-yl)-2-(diethoxyphosphinyl)eth-1-yl]-4[R]-methyl-1,3,2-dioxaphospholane-2-oxide;
- 2[2-(5-[3,*N*-phthalimidopropoxy]pyrid-2-yl)-2-(diethoxyphosphinyl)eth-1-yl]-1,3,2-dioxaphospholane-2-oxide;
- 20 2[2-(5-[4,*N*-phthalimidobutoxy]pyrid-2-yl)-2-(diethoxyphosphinyl)eth-1-yl]-4[R]-methyl-1,3,2-dioxaphospholane-2-oxide;
- 2[2-(5-[2-{*N*-methyl-*N*-pyrid-2-ylamino}ethoxy]benzothien-2-yl)-2-(diethoxyphosphinyl)eth-1-yl]-1,3,2-dioxaphospholane-2-oxide;

- 2[2-(5-[*N*-(2-{*N*-methyl-*N*-pyrid-2-ylamino} ethyl)-*N*-methylamino]benzothien-2-yl)-2-(diethoxyphosphinyl)eth-1-yl]-4[R]-methyl-1,3,2-dioxaphospholane-2-oxide;
- 2[2-(5-[3-{*N*-methyl-*N*-pyrid-2-ylamino}-1-oxoprop-1-yl]benzothien-2-yl)-2-(diethoxyphosphinyl)eth-1-yl]-1,3,2-dioxaphosphinane-2-oxide;
- 5 2[2-(5-[2-{5-methyl-2-phenyloxazol-4-yl} ethoxy]benzothien-2-yl)-2-(diethoxyphosphinyl)eth-1-yl]-1,3,2-dioxaphosphinane-2-oxide;
- 2[2-(5-[*N*-(2-{5-methyl-2-phenyloxazol-4-yl} ethyl)-*N*-methylamino]benzothien-2-yl)-2-(diethoxyphosphinyl)eth-1-yl]-1,3,2-dioxaphosphinane-2-oxide;
- 2[2-(5-[2-{5-methyl-2-phenylthiazol-4-yl} ethoxy]benzothien-2-yl)-2-
- 10 (diethoxyphosphinyl)eth-1-yl]-1,3,2-dioxaphosphinane-2-oxide;
- 2[2-(5-[3-{5-methyl-2-phenylthiazol-4-yl}-1-oxoprop-1-yl]benzothien-2-yl)-1-(diethoxyphosphinyl)eth-1-yl]-1,3,2-dioxaphospholane-2-oxide;
- 2[2-(5-[2-{5-methyl-2-pyrid-4-yloxazol-4-yl} ethoxy]benzothien-2-yl)-1-(diethoxyphosphinyl)eth-1-yl]-1,3,2-dioxaphospholane-2-oxide;
- 15 2[2-(5-[2-{5-methyl-2-pyrid-4-ylthiazol-4-yl} ethoxy]benzothien-2-yl)-1-(diethoxyphosphinyl)eth-1-yl]-1,3,2-dioxaphospholane-2-oxide;
- 2[2-(5-[3-{5-methyl-2-pyrid-4-yloxazol-4-yl}-1-oxoprop-1-yl]benzothien-2-yl)-1-(diethoxyphosphinyl)eth-1-yl]-1,3,2-dioxaphospholane-2-oxide;
- N,N,N',N'*-Tetramethyl-1 (5-[*N*-(2-{5-methyl-2-pyrid-4-ylthiazol-4-yl} ethyl)-*N*-
- 20 methylamino]benzothien-2-yl)-1-hydroxymethylphosphondiamide;
- N,N'*-Diethyl 1-(5-[2-{4-(4-trifluoromethylphenyl)phenoxy} ethoxy]benzothien-2-yl)-1-hydroxymethylphosphondiamide;
- 2-[1-hydroxy-1-(5-[*N*-(2-{4-(4-trifluoromethylphenyl)phenoxy} ethyl)-*N*-methylamino]benzothien-2-yl)methyl]-[4*S*,5*S*]-dimethyl-1,3,2-diazaphospholidine-2-
- 25 oxide;

- 2-[1-hydroxy-1-(5-[3-{4-(4-trifluoromethylphenyl)phenoxy}-1-oxoprop-1-yl]benzothien-2-yl)methyl]-1,3,5,5-tetramethyl-1,3,2-diazaphosphinane-2-oxide;
- 2-[1-hydroxy-1-(5-[2-{1-[4-(2-trifluoromethylphenyl)phenylmethyl]-3-hexylureido}ethyl]benzothien-2-yl)methyl]-[4S]-ethyl-1,3,2-oxazaphospholidine-2-oxide;
- 5 2-[1-hydroxy-1-(5-[2-{1-butyl-3-(5-methoxypyrid-2-yl)ureido}ethyl]benzothien-2-yl)methyl]-[4R]methyl-1,3,2-oxazaphosphinane-2-oxide;
- N,N,N',N'*-Tetramethyl-1 (5-[3-{4-acetyl-3-hydroxy-2-propylphenoxy}propoxy]benzothien-2-yl)-1-hydroxymethylphosphondiamide;
- 10 *N,N'*-Diethyl 1-(5-[2-{4*H*-3-oxobenzo[1,4]oxazin-2-yl}ethoxy]benzothien-2-yl)-1-hydroxymethylphosphondiamide;
- 2-[1-hydroxy-1-(5-[3,*N*-phthalimidopropoxy]benzothien-2-yl)methyl]-[4S,5S]-dimethyl-1,3,2-diazaphospholidine-2-oxide;
- 2-[1-hydroxy-1-(5-[4,*N*-phthalimidobutoxy]benzothien-2-yl)methyl]-1,3,5,5-tetramethyl-1,3,2-diazaphosphinane-2-oxide;
- 15 2-[1-hydroxy-1-(4-[2-{*N*-methyl-*N*-pyrid-2-ylamino}ethoxy]thiazol-2-yl)methyl]-[4S]-ethyl-1,3,2-oxazaphospholidine-2-oxide;
- 2-[1-hydroxy-1-(4-[*N*-(2-{*N*-methyl-*N*-pyrid-2-ylamino}ethyl)-*N*-methylamino]thiazol-2-yl)methyl]-[4R]methyl-1,3,2-oxazaphosphinane-2-oxide;
- 20 *N,N,N',N'*-Tetramethyl 1-(4-[3-{*N*-methyl-*N*-pyrid-2-ylamino}-1-oxoprop-1-yl]thiazol-2-yl)-1-(bis[*N,N*-dimethylamino]phosphoryloxy)methylphosphondiamide;
- N,N'*-Diethyl 1-(4-[2-{5-methyl-2-phenyloxazol-4-yl}ethoxy]thiazol-2-yl)-1-(bis[*N*-ethylamino]phosphoryloxy)methylphosphondiamide;

- 2-[1-{([4S,5S]-dimethyl-2-oxido-1,3,2-diazaphospholidin-2-yl)oxy}-1-(4-[*N*-(2-{5-methyl-2-phenyloxazol-4-yl}ethyl)-*N*-methylamino]thiazol-2-yl)methyl]-[4S,5S]-dimethyl-1,3,2-diazaphospholidine-2-oxide;
- 2-[1-{(1,3,5,5-tetramethyl-2-oxido-1,3,2-diazaphosphinan-2-yl)oxy}-1-(4-[2-{5-methyl-2-phenylthiazol-4-yl}ethoxy]thiazol-2-yl)methyl]-1,3,5,5-tetramethyl-1,3,2-diazaphosphinane-2-oxide;
- 2-[1-{(4S)-ethyl-2-oxido-1,3,2-oxazaphospholidin-2-yl)oxy}-1-(4-[3-{5-methyl-2-phenylthiazol-4-yl}-1-oxoprop-1-yl]thiazol-2-yl)methyl]-[4S]-ethyl-1,3,2-oxazaphospholidine-2-oxide;
- 2-[1-{(4R)methyl-1,3,2-oxazaphosphinan-2-yl)oxy}-1-(4-[2-{5-methyl-2-pyrid-4-yloxazol-4-yl}ethoxy]thiazol-2-yl)methyl]-[4R]methyl-1,3,2-oxazaphosphinane-2-oxide;
- N,N,N',N'*-Tetramethyl 1-(4-[2-{5-methyl-2-pyrid-4-ylthiazol-4-yl}ethoxy]thiazol-2-yl)-1-(bis[*N,N*-dimethylamino]phosphoryloxy)methylphosphondiamide;
- N,N'*-Diethyl 1-(4-[3-{5-methyl-2-pyrid-4-yloxazol-4-yl}-1-oxoprop-1-yl]thiazol-2-yl)-1-(bis[*N*-ethylamino]phosphoryloxy)methylphosphondiamide;
- 2-[1-{([4S,5S]-dimethyl-2-oxido-1,3,2-diazaphospholidin-2-yl)oxy}-1-(4-[*N*-(2-{5-methyl-2-pyrid-4-ylthiazol-4-yl}ethyl)-*N*-methylamino]thiazol-2-yl)methyl]-[4S,5S]-dimethyl-1,3,2-diazaphospholidine-2-oxide;
- 2-[1-{(1,3,5,5-tetramethyl-2-oxido-1,3,2-diazaphosphinan-2-yl)oxy}-1-(4-[2-{4-(4-trifluoromethylphenyl)phenoxy}ethoxy]thiazol-2-yl)methyl]-1,3,5,5-tetramethyl-1,3,2-diazaphosphinane-2-oxide;
- 2-[1-{(4S)-ethyl-2-oxido-1,3,2-oxazaphospholidin-2-yl)oxy}-1-(4-[*N*-(2-{4-(4-trifluoromethylphenyl)phenoxy}ethyl)-*N*-methylamino]thiazol-2-yl)methyl]-[4S]-ethyl-1,3,2-oxazaphospholidine-2-oxide;



- 2-[1-{([4R]methyl-1,3,2-oxazaphosphinan-2-yl)oxy}-1-(4-[3-{4-(4-trifluoromethylphenyl)phenoxy}-1-oxoprop-1-yl]thiazol-2-yl)methyl]-[4R]methyl-1,3,2-oxazaphosphinane-2-oxide;
- 1-(4-[2-{1-[4-(2-trifluoromethylphenyl)phenylmethyl]-3-hexylureido}ethyl]thiazol-2-yl)-1,1-bis(bis[*N,N*-dimethylamino]phosphoryl)methane;
- 1-(4-[2-{1-butyl-3-(5-methoxypyrid-2-yl)ureido}ethyl]thiazol-2-yl)-1,1-bis(bis[*N*-ethylamino]phosphoryl)methane;
- 1-(4-[3-{4-acetyl-3-hydroxy-2-propylphenoxy}propoxy]thiazol-2-yl)-1,1-bis([4*S*,5*S*]-dimethyl-2-oxido-1,3,2-diazaphospholidin-2-yl)methane;
- 1-(4-[2-{4*H*-3-oxobenzo[1,4]oxazin-2-yl}ethoxy]thiazol-2-yl)-1,1-bis(1,3,5,5-tetramethyl-2-oxido-1,3,2-diazaphosphinan-2-yl)methane;
- 1-(4-[3,*N*-phthalimidopropoxy]thiazol-2-yl)-1,1-bis ([4*S*]-ethyl-2-oxido-1,3,2-oxazaphospholidin-2-yl)methane;
- 1-(4-[4,*N*-phthalimidobutoxy]thiazol-2-yl)-1,1-bis ([4*R*]-methyl-2-oxido-1,3,2-oxazaphosphinan-2-yl)methane;
- 1-(6-[2-{*N*-methyl-*N*-pyrid-2-ylamino}ethoxy]-3-methoxyquinolin-2-yl)-1,1-bis(bis[*N,N*-dimethylamino]phosphoryl)methane;
- 1-(6-[*N*-(2-{*N*-methyl-*N*-pyrid-2-ylamino}ethyl)-*N*-methylamino]-3-methoxyquinolin-2-yl)-1,1-bis(bis[*N*-ethylamino]phosphoryl)methane;
- 1-(6-[3-{*N*-methyl-*N*-pyrid-2-ylamino}-1-oxoprop-1-yl]-3-methoxyquinolin-2-yl)-1,1-bis([4*S*,5*S*]-dimethyl-2-oxido-1,3,2-diazaphospholidin-2-yl)methane;
- 1-(6-[2-{5-methyl-2-phenyloxazol-4-yl}ethoxy]-3-methoxyquinolin-2-yl)-1,1-bis(1,3,5,5-tetramethyl-2-oxido-1,3,2-diazaphosphinan-2-yl)methane;
- 1-(6-[*N*-(2-{5-methyl-2-phenyloxazol-4-yl}ethyl)-*N*-methylamino]-3-methoxyquinolin-2-yl)-1,1-bis ([4*S*]-ethyl-2-oxido-1,3,2-oxazaphospholidin-2-yl)methane;

- 1-(6-[2-{5-methyl-2-phenylthiazol-4-yl}ethoxy]-3-methoxyquinolin-2-yl)-1,1-bis  
 ([4R]methyl-2-oxido-1,3,2-oxazaphosphinan-2-yl)methane;
- 1-(6-[3-{5-methyl-2-phenylthiazol-4-yl}-1-oxoprop-1-yl]-3-methoxyquinolin-2-yl)-1,2-  
 bis(bis[*N,N*-dimethylamino]phosphoryl)ethane;
- 5 1-(6-[2-{5-methyl-2-pyrid-4-yloxazol-4-yl}ethoxy]-3-methoxyquinolin-2-yl)-1,2-  
 bis(bis[*N*-ethylamino]phosphoryl)ethane;
- 1-(6-[2-{5-methyl-2-pyrid-4-ylthiazol-4-yl}ethoxy]-3-methoxyquinolin-2-yl)-1,2-  
 bis([4S,5S]-dimethyl-2-oxido-1,3,2-diazaphospholidin-2-yl)ethane;
- 1-(6-[3-{5-methyl-2-pyrid-4-yloxazol-4-yl}-1-oxoprop-1-yl]-3-methoxyquinolin-2-yl)-  
 10 1,2-bis(1,3,5,5-tetramethyl-2-oxido-1,3,2-diazaphosphinan-2-yl)ethane;
- 1-(6-[*N*-(2-{5-methyl-2-pyrid-4-ylthiazol-4-yl}ethyl)-*N*-methylamino]-3-  
 methoxyquinolin-2-yl)-1,2-bis ([4S]-ethyl-2-oxido-1,3,2-oxazaphospholidin-2-  
 yl)ethane;
- 1-(6-[2-{4-(4-trifluoromethylphenyl)phenoxy}ethoxy]-3-methoxyquinolin-2-yl)-1,2-bis  
 15 ([4R]methyl-2-oxido-1,3,2-oxazaphosphinan-2-yl)ethane;
- 1-(6-[*N*-(2-{4-(4-trifluoromethylphenyl)phenoxy}ethyl)-*N*-methylamino]-3-  
 methoxyquinolin-2-yl)-1,2-bis(bis[*N,N*-dimethylamino]phosphoryl)ethane;
- 1-(6-[3-{4-(4-trifluoromethylphenyl)phenoxy}-1-oxoprop-1-yl]-3-methoxyquinolin-2-yl)-  
 1,2-bis(bis[*N*-ethylamino]phosphoryl)ethane;
- 20 1-(6-[2-{1-[4-(2-trifluoromethylphenyl)phenylmethyl]-3-hexylureido}ethyl]-3-  
 methoxyquinolin-2-yl)-1,2-bis([4S,5S]-dimethyl-2-oxido-1,3,2-diazaphospholidin-2-  
 yl)ethane;
- 1-(6-[2-{1-butyl-3-(5-methoxypyrid-2-yl)ureido}ethyl]-3-methoxyquinolin-2-yl)-1,2-  
 bis(1,3,5,5-tetramethyl-2-oxido-1,3,2-diazaphosphinan-2-yl)ethane;

- 1-(6-[3-{4-acetyl-3-hydroxy-2-propylphenoxy}propoxy]-3-methoxyquinolin-2-yl)-1,2-bis  
 ([4S]-ethyl-2-oxido-1,3,2-oxazaphospholidin-2-yl)ethane;
- 1-(6-[3,*N*-phthalimidopropoxy]-3-methoxyquinolin-2-yl)-1,2-bis ([4R]methyl-2-oxido-  
 1,3,2-oxazaphosphinan-2-yl)ethane;
- 5 2-(6-[4,*N*-phthalimidobutoxy]-3-methoxyquinolin-2-yl)-1,1-bis(bis[*N,N*-  
 dimethylamino]phosphoryl)ethane;
- 2-(5-[2-{*N*-methyl-*N*-pyrid-2-ylamino}ethoxy]thien-2-yl)-1,1-bis(bis[*N*-  
 ethylamino]phosphoryl)ethane;
- 2-(5-[*N*-(2-{*N*-methyl-*N*-pyrid-2-ylamino}ethyl)-*N*-methylamino]thien-2-yl)-1,1-  
 10 bis([4S,5S]-dimethyl-2-oxido-1,3,2-diazaphospholidin-2-yl)ethane;
- 2-(5-[3-{*N*-methyl-*N*-pyrid-2-ylamino}-1-oxoprop-1-yl]thien-2-yl)-1,1-bis(1,3,5,5-  
 tetramethyl-2-oxido-1,3,2-diazaphosphinan-2-yl)ethane;
- 2-(5-[2-{5-methyl-2-phenyloxazol-4-yl}ethoxy]thien-2-yl)-1,1-bis ([4S]-ethyl-2-oxido-  
 1,3,2-oxazaphospholidin-2-yl)ethane;
- 15 2-(5-[*N*-(2-{5-methyl-2-phenyloxazol-4-yl}ethyl)-*N*-methylamino]thien-2-yl)-1,1-bis  
 ([4R]methyl-2-oxido-1,3,2-oxazaphosphinan-2-yl)ethane;
- 2-(5-[2-{5-methyl-2-phenylthiazol-4-yl}ethoxy]thien-2-yl)-1,1-bis(bis[*N,N*-  
 dimethylamino]phosphoryl)ethane;
- 2-(5-[3-{5-methyl-2-phenylthiazol-4-yl}-1-oxoprop-1-yl]thien-2-yl)-1,1-bis(bis[*N*-  
 20 ethylamino]phosphoryl)ethane;
- 2-(5-[2-{5-methyl-2-pyrid-4-ylloxazol-4-yl}ethoxy]thien-2-yl)-1,1-bis([4S,5S]-dimethyl-  
 2-oxido-1,3,2-diazaphospholidin-2-yl)ethane;
- 2-(5-[2-{5-methyl-2-pyrid-4-ylthiazol-4-yl}ethoxy]thien-2-yl)-1,1-bis(1,3,5,5-  
 tetramethyl-2-oxido-1,3,2-diazaphosphinan-2-yl)ethane;

- 2-(5-[3-{5-methyl-2-pyrid-4-yl}oxazol-4-yl]-1-oxoprop-1-yl]thien-2-yl)-1,1-bis ([4S]-ethyl-2-oxido-1,3,2-oxazaphospholidin-2-yl)ethane;
- 2-(5-[*N*-(2-{5-methyl-2-pyrid-4-yl}thiazol-4-yl)ethyl)-*N*-methylamino]thien-2-yl)-1,1-bis ([4R]methyl-2-oxido-1,3,2-oxazaphosphinan-2-yl)ethane;
- 5 1-[*N*-(5-[2-{4-(4-trifluoromethylphenyl)phenoxy}ethoxy]thien-2-yl)amino]-1,1-bis(bis[*N,N*-dimethylamino]phosphoryl)methane;
- 1-[*N*-(5-[*N*-(2-{4-(4-trifluoromethylphenyl)phenoxy}ethyl)-*N*-methylamino]thien-2-yl)amino]-1,1-bis(bis[*N*-ethylamino]phosphoryl)methane;
- 1-[*N*-(5-[3-{4-(4-trifluoromethylphenyl)phenoxy}-1-oxoprop-1-yl]thien-2-yl)amino]-1,1-bis([4S,5S]-dimethyl-2-oxido-1,3,2-diazaphospholidin-2-yl)methane;
- 10 1-[*N*-(5-[2-{1-[4-(2-trifluoromethylphenyl)phenylmethyl]-3-hexylureido}ethyl]thien-2-yl)amino]-1,1-bis(1,3,5,5-tetramethyl-2-oxido-1,3,2-diazaphosphinan-2-yl)methane;
- 1-[*N*-(5-[2-{1-butyl-3-(5-methoxypyrid-2-yl)ureido}ethyl]thien-2-yl)amino]-1,1-bis ([4S]-ethyl-2-oxido-1,3,2-oxazaphospholidin-2-yl)methane;
- 15 1-[*N*-(5-[3-{4-acetyl-3-hydroxy-2-propylphenoxy}propoxy]thien-2-yl)amino]-1,1-bis ([4R]methyl-2-oxido-1,3,2-oxazaphosphinan-2-yl)methane;
- 1-[*N*-(5-[2-{4*H*-3-oxobenzo[1,4]oxazin-2-yl}ethoxy]thien-2-yl)amino]-1,1-bis(bis[*N,N*-dimethylamino]phosphoryl)methane;
- 1-[*N*-(5-[3,*N*-phthalimidopropoxy]thien-2-yl)amino]-1,1-bis(bis[*N*-ethylamino]phosphoryl)methane;
- 20 1-[*N*-(5-[4,*N*-phthalimidobutoxy]thien-2-yl)amino]-1,1-bis([4S,5S]-dimethyl-2-oxido-1,3,2-diazaphospholidin-2-yl)methane;
- 1-[*N*-(4-[2-{*N*-methyl-*N*-pyrid-2-ylamino}ethoxy]-3-fluorophenyl)amino]-1,1-bis(1,3,5,5-tetramethyl-2-oxido-1,3,2-diazaphosphinan-2-yl)methane;

- 1-[*N*-(4-[*N*-(2-{*N*-methyl-*N*-pyrid-2-ylamino} ethyl)-*N*-methylaminocarbonyl]-3-fluorophenyl)amino]-1,1-bis ([4*S*]-ethyl-2-oxido-1,3,2-oxazaphospholidin-2-yl)methane;
- 1-[*N*-(4-[3-{*N*-methyl-*N*-pyrid-2-ylamino}-1-oxoprop-1-yl]-3-fluorophenyl)amino]-1,1-bis ([4*R*]-methyl-2-oxido-1,3,2-oxazaphosphinan-2-yl)methane;
- 2-[1-(Bis[*N*-ethylamino]phosphoryloxy)-1-(4-[2-{5-methyl-2-phenyloxazol-4-yl} ethoxy]-3-fluorophenyl)methyl]-[4*S*,5*S*]-dimethyl-1,3,2-diazaphospholidine-2-oxide;
- 2-[1-(Bis[*N*-ethylamino]phosphoryl)-1-(4-[*N*-(2-{5-methyl-2-phenyloxazol-4-yl} ethyl)-*N*-methylaminocarbonyl]-3-fluorophenyl)methoxy]-[4*S*,5*S*]-dimethyl-1,3,2-diazaphospholidine-2-oxide;
- 2-[1-(Bis[*N*-ethylamino]phosphoryl)-1-(4-[2-{5-methyl-2-phenylthiazol-4-yl} ethoxy]-3-fluorophenyl)methyl]-1,3,5,5-tetramethyl-1,3,2-diazaphosphinane-2-oxide;
- 2-[1-(Bis[*N*-ethylamino]phosphoryl)-2-(4-[3-{5-methyl-2-phenylthiazol-4-yl}-1-oxoprop-1-yl]-3-fluorophenyl)ethen-1-yl]-[4*S*]-ethyl-1,3,2-oxazaphospholidine-2-oxide;
- 2-[1-(Bis[*N*-ethylamino]phosphoryl)-2-(4-[2-{5-methyl-2-pyrid-4-yloxazol-4-yl} ethoxy]-3-fluorophenyl)eth-1-yl]-[4*R*]-methyl-1,3,2-oxazaphosphinane-2-oxide;
- 2-[2-(Bis[*N*-ethylamino]phosphoryl)-2-(4-[2-{5-methyl-2-pyrid-4-ylthiazol-4-yl} ethoxy]-3-fluorophenyl)eth-1-yl]-1,3,5,5-tetramethyl-1,3,2-diazaphosphinane-2-oxide;
- 2-[2-(Bis[*N*-ethylamino]phosphoryl)-1-(4-[3-{5-methyl-2-pyrid-4-yloxazol-4-yl}-1-oxoprop-1-yl]-3-fluorophenyl)eth-1-yl]-[4*S*]-ethyl-1,3,2-oxazaphospholidine-2-oxide;
- 2-[1-(Bis[*N*-ethylamino]phosphoryloxy)-1-(4-[*N*-(2-{5-methyl-2-pyrid-4-ylthiazol-4-yl} ethyl)-*N*-methylaminocarbonyl]-3-fluorophenyl)methyl]-[4*S*,5*S*]-dimethyl-1,3,2-diazaphospholidine-2-oxide;

- 2-[1-(Bis[*N*-ethylamino]phosphoryl)-1-(4-[2-{4-(4-trifluoromethylphenyl)phenoxy}ethoxy]-3-fluorophenyl)methoxy]-[4*S*,5*S*]-dimethyl-1,3,2-diazaphospholidine-2-oxide;
- 2-[1-(Bis[*N*-ethylamino]phosphoryl)-1-(4-[*N*-(2-{4-(4-trifluoromethylphenyl)phenoxy}ethyl)-*N*-methylaminocarbonyl]-3-fluorophenyl)methyl]-1,3,5,5-tetramethyl-1,3,2-diazaphosphinane-2-oxide;
- 2-[1-(Bis[*N*-ethylamino]phosphoryl)-2-(4-[3-{4-(4-trifluoromethylphenyl)phenoxy}-1-oxoprop-1-yl]-3-fluorophenyl)ethen-1-yl]-[4*S*]-ethyl-1,3,2-oxazaphospholidine-2-oxide;
- 2-[1-(Bis[*N*-ethylamino]phosphoryl)-2-(4-[2-{1-[4-(2-trifluoromethylphenyl)phenylmethyl]-3-hexylureido}ethyl]-3-fluorophenyl)eth-1-yl]-[4*R*]-methyl-1,3,2-oxazaphosphinane-2-oxide;
- 2-[2-(Bis[*N*-ethylamino]phosphoryl)-2-(4-[2-{1-butyl-3-(5-methoxypyrid-2-yl)ureido}ethyl]-3-fluorophenyl)eth-1-yl]-1,3,5,5-tetramethyl-1,3,2-diazaphosphinane-2-oxide;
- 2-[2-(Bis[*N*-ethylamino]phosphoryl)-1-(4-[3-{4-acetyl-3-hydroxy-2-propylphenoxy}propoxy]-3-fluorophenyl)eth-1-yl]-[4*S*]-ethyl-1,3,2-oxazaphospholidine-2-oxide;
- 2-[1-(Diethoxyphosphoryloxy)-1-(4-[2-{4*H*-3-oxobenzo[1,4]oxazin-2-yl}ethoxy]-3-fluorophenyl)methyl]-[4*S*,5*S*]-dimethyl-1,3,2-diazaphospholidine-2-oxide;
- 2-[1-(Diethoxyphosphoryl)-1-(4-[3,*N*-phthalimidopropoxy]-3-fluorophenyl)methoxy]-[4*S*,5*S*]-dimethyl-1,3,2-diazaphospholidine-2-oxide;
- 2-[1-(Diethoxyphosphoryl)-1-(4-[4,*N*-phthalimidobutoxy]-3-fluorophenyl)methyl]-1,3,5,5-tetramethyl-1,3,2-diazaphosphinane-2-oxide;

- 2-[1-(Diethoxyphosphoryl)-2-(3-[3-{*N*-methyl-*N*-pyrid-2-ylamino}propoxy]-4-fluorophenyl)ethen-1-yl]-[4S]-ethyl-1,3,2-oxazaphospholidine-2-oxide;
- 2-[1-(Diethoxyphosphoryl)-2-(3-[*N*-(3-{*N*-methyl-*N*-pyrid-2-ylamino}propyl)-*N*-methylamino]-4-fluorophenyl)eth-1-yl]-[4R]methyl-1,3,2-oxazaphosphinane-2-oxide;
- 5 2-[2-(Diethoxyphosphoryl)-2-(3-[3-{*N*-methyl-*N*-pyrid-2-ylamino}-1-oxoprop-1-ylamino]-4-fluorophenyl)eth-1-yl]-1,3,5,5-tetramethyl-1,3,2-diazaphosphinane-2-oxide;
- 2-[2-(Diethoxyphosphoryl)-1-(3-[3-{5-methyl-2-phenyloxazol-4-yl}propoxy]-4-fluorophenyl)eth-1-yl]-[4S]-ethyl-1,3,2-oxazaphospholidine-2-oxide;
- 10 2-[1-(Diethoxyphosphoryloxy)-1-(3-[*N*-(2-{5-methyl-2-phenyloxazol-4-yl}ethyl)-*N*-methylaminocarbonyl]-4-methoxyphenyl)methyl]-[4S,5S]-dimethyl-1,3,2-diazaphospholidine-2-oxide;
- 2-[1-(Diethoxyphosphoryl)-1-(3-[3-{5-methyl-2-phenylthiazol-4-yl}propoxy]-4-fluorophenyl)methoxy]-[4S,5S]-dimethyl-1,3,2-diazaphospholidine-2-oxide;
- 15 2-[1-(Diethoxyphosphoryl)-1-(3-[3-{5-methyl-2-phenylthiazol-4-yl}-1-oxoprop-1-yl]-4-fluorophenyl)methyl]-1,3,5,5-tetramethyl-1,3,2-diazaphosphinane-2-oxide;
- 2-[1-(Diethoxyphosphoryl)-2-(3-[4-{5-methyl-2-pyrid-4-yloxazol-4-yl}butoxy]-4-fluorophenyl)ethen-1-yl]-[4S]-ethyl-1,3,2-oxazaphospholidine-2-oxide;
- 2-[1-(Diethoxyphosphoryl)-2-(3-[3-{5-methyl-2-pyrid-4-ylthiazol-4-yl}propoxy]-4-fluorophenyl)eth-1-yl]-[4R]methyl-1,3,2-oxazaphosphinane-2-oxide;
- 20 2-[2-(Diethoxyphosphoryl)-2-(3-[3-{5-methyl-2-pyrid-4-yloxazol-4-yl}-1-oxoprop-1-ylthio]-4-fluorophenyl)eth-1-yl]-1,3,5,5-tetramethyl-1,3,2-diazaphosphinane-2-oxide;
- 2-[2-(Diethoxyphosphoryl)-1-(3-[*N*-(3-{5-methyl-2-pyrid-4-ylthiazol-4-yl}propyl)-*N*-methylamino]-4-fluorophenyl)eth-1-yl]-[4S]-ethyl-1,3,2-oxazaphospholidine-2-oxide.

In an even more preferred embodiment of this aspect, the compound of Formula (I) is selected from:

- Diethyl 1-(diethoxyphosphinyloxy)-1-(4-[2-{*N*-methyl-*N*-pyrid-2-ylamino}ethoxy]-3-fluorophenyl)methylphosphonate;
- 5 Diethyl 1-(diethoxyphosphinyloxy)-1-(4-[3,*N*-phthalimidopropoxy]-3-fluorophenyl)methylphosphonate;
- Diethyl 1-(diethoxyphosphinyloxy)-1-(4-[2-{5-methyl-2-phenyloxazol-4-yl}ethoxy]-3-fluorophenyl)methylphosphonate;
- Diethyl 1-(diethoxyphosphinyloxy)-1-(3-[3-{*N*-methyl-*N*-pyrid-2-ylamino}propoxy]-4-10 fluorophenyl)methylphosphonate;
- Diethyl 1-(diethoxyphosphinyloxy)-1-(3-[4-{*N*-methyl-*N*-pyrid-2-ylamino}butoxy]-4-fluorophenyl)methylphosphonate;
- Diethyl 1-(diethoxyphosphinyloxy)-1-(3-[4,*N*-phthalimidobutoxy]-4-fluorophenyl)methylphosphonate;
- 15 Diethyl 1-(diethoxyphosphinyloxy)-1-(3-[5,*N*-phthalimidopentoxy]-4-fluorophenyl)methylphosphonate;
- Diethyl 1-(diethoxyphosphinyloxy)-1-(3-[4-{5-methyl-2-pyrid-4-yloxazol-4-yl}butoxy]-4-fluorophenyl)methylphosphonate;
- Diethyl 1-(diethoxyphosphinyloxy)-1-(3-[5-{5-methyl-2-pyrid-4-yloxazol-4-yl}pentoxy]-20 4-fluorophenyl)methylphosphonate;
- 1-(4-[2-{*N*-methyl-*N*-pyrid-2-ylamino}ethoxy]-3-fluorophenyl)-1,1-bis([4*R*,5*S*]-dimethyl-2-oxido-1,3,2-dioxaphospholan-2-yl)methane;
- 1-(4-[3,*N*-phthalimidopropoxy]-3-fluorophenyl)-1,1-bis([4*R*,5*S*]-dimethyl-2-oxido-1,3,2-dioxaphospholan-2-yl)methane;



- 1-(4-[2-{5-methyl-2-phenyloxazol-4-yl}ethoxy]-3-fluorophenyl)-1,1-bis([4R,5S]-dimethyl-2-oxido-1,3,2-dioxaphospholan-2-yl)methane;
- 1-(3-[3-{*N*-methyl-*N*-pyrid-2-ylamino}propoxy]-4-fluorophenyl)-1,1-bis([4R,5S]-dimethyl-2-oxido-1,3,2-dioxaphospholan-2-yl)methane;
- 5 1-(3-[4-{*N*-methyl-*N*-pyrid-2-ylamino}butoxy]-4-fluorophenyl)-1,1-bis([4R,5S]-dimethyl-2-oxido-1,3,2-dioxaphospholan-2-yl)methane;
- 1-(3-[4,*N*-phthalimidobutoxy]-4-fluorophenyl)-1,1-bis([4R,5S]-dimethyl-2-oxido-1,3,2-dioxaphospholan-2-yl)methane;
- 1-(3-[5,*N*-phthalimidopentoxy]-4-fluorophenyl)-1,1-bis([4R,5S]-dimethyl-2-oxido-1,3,2-dioxaphospholan-2-yl)methane;
- 10 1-(3-[4-{5-methyl-2-pyrid-4-yloxazol-4-yl}butoxy]-4-fluorophenyl)-1,1-bis([4R,5S]-dimethyl-2-oxido-1,3,2-dioxaphospholan-2-yl)methane;
- 1-(3-[5-{5-methyl-2-pyrid-4-yloxazol-4-yl}pentoxy]-4-fluorophenyl)-1,1-bis([4R,5S]-dimethyl-2-oxido-1,3,2-dioxaphospholan-2-yl)methane;
- 15 *N,N,N',N'*-Tetramethyl 1-(4-[2-{*N*-methyl-*N*-pyrid-2-ylamino}ethoxy]-3-fluorophenyl)-1-hydroxymethylphosphondiamide;
- N,N,N',N'*-Tetramethyl 1-(4-[3,*N*-phthalimidopropoxy]-3-fluorophenyl)-1-hydroxymethylphosphondiamide;
- N,N,N',N'*-Tetramethyl 1-(4-[2-{5-methyl-2-phenyloxazol-4-yl}ethoxy]-3-fluorophenyl)-1-hydroxymethylphosphondiamide;
- 20 2-[1-hydroxy-1-(4-[2-{*N*-methyl-*N*-pyrid-2-ylamino}ethoxy]-3-fluorophenyl)methyl]-[4S]-(1-methylethyl)-1,3,2-oxazaphospholidine-2-oxide;
- 2-[1-hydroxy-1-(4-[3,*N*-phthalimidopropoxy]-3-fluorophenyl)methyl]-[4S]-(1-methylethyl)-1,3,2-oxazaphospholidine-2-oxide;

2-[1-hydroxy-1-(4-[2-{5-methyl-2-phenyloxazol-4-yl}ethoxy]-3-fluorophenyl)methyl]-  
[4S]-(1-methylethyl)-1,3,2-oxazaphospholidine-2-oxide;

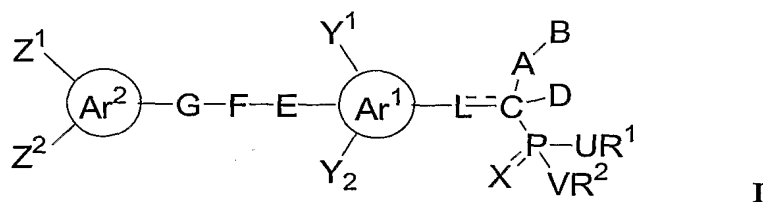
1-[*N*-(4-[2-{*N*-methyl-*N*-pyrid-2-ylamino}ethoxy]-3-fluorophenyl)amino]-1,1-bis(bis[*N*-  
ethylamino]phosphoryl)methane;

5 1-[*N*-(4-[3,*N*-phthalimidopropoxy]-3-fluorophenyl)amino]-1,1-bis(bis[*N*-  
ethylamino]phosphoryl)methane; and

1-[*N*-(4-[2-{5-methyl-2-phenyloxazol-4-yl}ethoxy]-3-fluorophenyl)amino]-1,1-  
bis(bis[*N*-ethylamino]phosphoryl)methane.

The compounds of Formula (I) may have asymmetric centers and occur as  
10 racemates, racemic mixtures and as individual diastereomers, or enantiomers. All  
isomeric forms are included within the scope of the present invention.

In another aspect, the invention relates to pharmaceutical formulations comprising  
a compound, or pharmaceutically acceptable salt thereof, of Formula (I):



15 wherein

A is a bond, O, CH<sub>2</sub>, CHF, CF<sub>2</sub>, or NR<sub>6</sub>;

B is H, C<sub>1</sub>-C<sub>6</sub> lower alkyl, or P(=X<sup>1</sup>)(UR<sup>3</sup>)(VR<sup>4</sup>);

D is a) H or lower alkyl, wherein the L=C bond is a single bond; or

b) OH, OCOR<sup>5</sup>, NH<sub>2</sub>, NR<sup>6</sup>R<sup>6a</sup>, or NHCOR<sup>5</sup>, wherein the L=C bond is a single  
20 bond, with the proviso that A is CH<sub>2</sub>, CHF, CF<sub>2</sub>;

L is a) NR<sup>6</sup>, CR<sup>7</sup>R<sup>8</sup>, -OCR<sup>7</sup>R<sup>8</sup>-, -NR<sup>6</sup>CR<sup>7</sup>R<sup>8</sup>-, or -S(O)<sub>m</sub>CR<sup>7</sup>R<sup>8</sup>-, wherein the L=C  
bond is a single bond; or

b)  $CR^7$ , wherein the  $L \equiv C$  bond is a double bond, with the proviso that D is absent when the  $L \equiv C$  bond is a double bond; or

c) absent, wherein C is covalently bonded by a single bond to  $Ar^1$ ;

$Ar^1$  and  $Ar^2$  are each independently mono- or bicyclic aromatic rings of 5-12 atoms, including, but not limited to phenyl, pyridyl, pyrimidyl, pyrazinyl, pyridazinyl, thienyl, furanyl, pyrrolyl, imidazolyl, pyrazolyl, oxazolyl, isoxazolyl, thiazolyl, isothiazolyl, 1,3,4-oxadiazolyl, 1,2,4-oxadiazolyl, 1,3,4-thiadiazolyl, 1,2,3-triazolyl, 1,3,4-triazolyl, 1,2,4-triazinyl, 1,3,5-triazinyl, benzofuranyl, benzothienyl, indolyl, indazolyl, benzimidazolyl, benzoxazolyl, benzoisoxazolyl, benzothiazolyl, benzoisothiazolyl, quinolinyl, isoquinolinyl, quinazolinyl, quinoxalinyl, naphthyridyl, or purinyl;

$Y^1$ ,  $Y^2$ , and  $Z^1$  are each independently a lone electron pair, H,  $C_1$ - $C_6$  lower alkyl,  $C_2$ - $C_6$  lower alkenyl,  $C_2$ - $C_6$  lower alkynyl,  $C_1$ - $C_6$  lower alkoxy,  $C_1$ - $C_6$  lower alkylamino,  $C_1$ - $C_6$  lower dialkylamino,  $C_2$ - $C_6$  lower cycloalkyl,  $C_4$ - $C_6$  lower cycloalkenyl,  $C_1$ - $C_6$  lower thioalkyl,  $C_1$ - $C_6$  lower sulfinylalkyl,  $C_1$ - $C_6$  lower sulfonylalkyl,  $C_1$ - $C_6$  lower acyloxy,  $C_1$ - $C_6$  lower acylamino with N substituted with  $R^6$ ,  $CH_2OR^5$ ,  $CH_2NR^6R^{6a}$ ,  $R^6$ ,  $R^6O$ , OH,  $NH_2$ , CN,  $NO_2$ , F, Cl, Br, I, or  $N_3$ ;

E is a bond,  $S(O)_m$ ,  $NR^6$ ,  $C=O$ ,  $CO_2$ ,  $CONR^6$ , O,  $-OC=O$ ,  $NR^6C=O$ ,  $NR^6CO_2$ ,  $OC=ONR^6$ ,  $OCO_2$ , or  $NR^6CONR^{6a}$ ;

F is  $(CH_2)_n$ ,  $(CH_2)_oO(CH_2)_p$ ,  $(CH_2)_oNR^6(CH_2)_p$ ,  $(CH_2)_oNR^6CO(CH_2)_p$ ,  $(CH_2)_oCONR^6(CH_2)_p$ ,  $(CH_2)_o(CR^6=CR^6)_q(CH_2)_p$ ,  $(CH_2)_o-(C \equiv C)_q-(CH_2)_p$ ;

G is a bond, O,  $NR^6$ , CO,  $CO_2$ , OCO,  $OCO_2$ ,  $S(O)_m$ ,  $CONR^6$ ,  $NR^6CO$ ,  $NR^6CO_2$ ,  $ONR^6$ ,  $NR^6CONR^{6a}$ , or G can optionally be attached to  $Ar^2$  at two contiguous C atoms to form a 5- to 7-membered partially saturated ring, which contains 0, 1, or 2 heteroatoms selected from the group consisting of O, N, and S;

X, X<sup>1</sup> are independently O or S

Z<sup>2</sup> is nothing, H or Ar<sup>1</sup> optionally substituted with Y<sup>1</sup> and Y<sup>2</sup>;

R<sup>1</sup>, R<sup>2</sup>, R<sup>3</sup>, and R<sup>4</sup>, are each independently selected from H, C<sub>1</sub>-C<sub>6</sub> lower alkyl, C<sub>3</sub>-C<sub>6</sub> lower alkenyl, C<sub>3</sub>-C<sub>6</sub> lower alkynyl, C<sub>3</sub>-C<sub>6</sub> lower cycloalkyl, C<sub>4</sub>-C<sub>6</sub> lower cycloalkenyl, or independently R<sup>1</sup> and R<sup>2</sup> or R<sup>3</sup> and R<sup>4</sup> can be taken together to form a 5 to 8-membered ring containing 2-7 carbon atoms, the 5 to 8-membered ring optionally substituted with zero to 3 substituents selected from the group C<sub>1</sub>-C<sub>4</sub> lower alkyl, C<sub>1</sub>-C<sub>4</sub> lower alkoxy, C<sub>1</sub>-C<sub>4</sub> lower alkylamino, C<sub>1</sub>-C<sub>4</sub> lower dialkylamino, amino, hydroxyl, hydroxymethyl, methoxymethyl, phenyl, substituted phenyl, benzyl, substituted benzyl;

U and V are each independently a bond, O or NR<sup>6</sup>;

R<sup>5</sup> R<sup>6</sup> and R<sup>6a</sup> are each independently C<sub>1</sub>-C<sub>6</sub> alkyl, C<sub>3</sub>-C<sub>6</sub> cycloalkyl, C<sub>3</sub>-C<sub>6</sub> alkenyl, C<sub>3</sub>-C<sub>6</sub> cycloalkenyl, C<sub>3</sub>-C<sub>6</sub> alkynyl, and H;

R<sup>7</sup> and R<sup>8</sup> are each independently H, C<sub>1</sub>-C<sub>4</sub> lower alkyl, or are taken together to form a saturated C<sub>3</sub>-C<sub>6</sub> carbocyclic ring;

R<sub>f</sub> is C<sub>1</sub>-C<sub>4</sub> straight or branched lower perfluoroalkyl;

all lower alkyl, alkenyl and alkynyl groups including those linked via heteroatoms can be straight chain or branched;

m is 0, 1, or 2;

n is 0, 1, 2, 3, 4, 5, or 6;

o is 0, 1, 2, 3, 4, 5, or 6;

p is 0, 1, 2, 3, 4, 5, or 6; and

q is 0, 1, 2, 3, 4, 5, or 6;

with the provisos that

when A is a bond or O, B is P(O)(OR<sup>3</sup>)(OR<sup>4</sup>), and D is selected from the group H, OH, OCOCH<sub>3</sub>, and NH<sub>2</sub>, and when R<sup>1</sup> = R<sup>2</sup> and R<sup>3</sup> = R<sup>4</sup>, and both are selected from the group H or unsubstituted C<sub>1</sub>-C<sub>4</sub> lower alkyl, and E and G are bonds, and F is (CH<sub>2</sub>)<sub>n</sub> where n is 0, and both Ar<sup>1</sup> and Ar<sup>2</sup> are phenyl, then at least one of Y<sup>1</sup>, Y<sup>2</sup>, Z<sup>1</sup>, or Z<sup>2</sup> must not be H; and

when A is a bond or CH<sub>2</sub>, and B is P(O)(OR<sup>3</sup>)(OR<sup>4</sup>), and either D is H or C<sub>1</sub>-C<sub>4</sub> lower alkyl where L is CH<sub>2</sub>, or D is absent, with L≡C taken together represent an ethenylidene group, and Ar<sup>1</sup> is phenyl, and E is a bond or O, and R<sup>1</sup> = R<sup>2</sup> and R<sup>3</sup> = R<sup>4</sup>, and both are drawn from the group H or C<sub>1</sub>-C<sub>6</sub> unsubstituted lower alkyl, then one of Y<sup>1</sup> and Y<sup>2</sup> must be other than H or unsubstituted C<sub>1</sub>-C<sub>4</sub> lower alkyl or unsubstituted C<sub>1</sub>-C<sub>4</sub> lower alkoxy; and

when A is O, and B is H or P(O)(OR<sup>3</sup>)(OR<sup>4</sup>), and R<sup>1</sup>, R<sup>2</sup>, R<sup>3</sup>, and R<sup>4</sup> are all selected from the group H or C<sub>1</sub>-C<sub>6</sub> unsubstituted lower alkyl, and D is H, and L is a bond, and Ar<sup>1</sup> is phenyl, and E is other than a bond or O, then one of Y<sup>1</sup> or Y<sup>2</sup> must be other than H, or C<sub>1</sub>-C<sub>4</sub> unsubstituted lower alkyl or C<sub>1</sub>-C<sub>4</sub> unsubstituted lower alkoxy;

and a pharmaceutically acceptable carrier, excipient, solvent, adjuvant or diluent.

In a preferred embodiment of this aspect, the pharmaceutical formulation comprises a compound of Formula (I) selected from:

Diethyl 1-(diethoxyphosphinyloxy)-1-(4-[2-{*N*-methyl-*N*-pyrid-2-ylamino}ethoxy]-3-fluorophenyl)methylphosphonate;

Diethyl 1-(diethoxyphosphinyloxy)-1-(4-[N-(2-{*N*-methyl-*N*-pyrid-2-ylamino}ethyl)-*N*-methylaminocarbonyl]-3-fluorophenyl)methylphosphonate;

Diethyl 1-(diethoxyphosphinyloxy)-1-(4-[3-{*N*-methyl-*N*-pyrid-2-ylamino}-1-oxoprop-1-yl]-3-fluorophenyl)methylphosphonate;

- Diethyl 1-(diethoxyphosphinyloxy)-1-(4-[2-{5-methyl-2-phenyloxazol-4-yl}ethoxy]-3-fluorophenyl)methylphosphonate;
- Diethyl 1-(diethoxyphosphinyloxy)-1-(4-[*N*-(2-{5-methyl-2-phenyloxazol-4-yl}ethyl)-*N*-methylaminocarbonyl]-3-fluorophenyl)methylphosphonate;
- 5 Diethyl 1-(diethoxyphosphinyloxy)-1-(4-[2-{5-methyl-2-phenylthiazol-4-yl}ethoxy]-3-fluorophenyl)methylphosphonate;
- Diethyl 1-(diethoxyphosphinyloxy)-1-(4-[3-{5-methyl-2-phenylthiazol-4-yl}-1-oxoprop-1-yl]-3-fluorophenyl)methylphosphonate;
- Diethyl 1-(diethoxyphosphinyloxy)-1-(4-[2-{5-methyl-2-pyrid-4-ylloxazol-4-yl}ethoxy]-
- 10 3-fluorophenyl)methylphosphonate;
- Diethyl 1-(diethoxyphosphinyloxy)-1-(4-[2-{5-methyl-2-pyrid-4-ylthiazol-4-yl}ethoxy]-3-fluorophenyl)methylphosphonate;
- Diethyl 1-(diethoxyphosphinyloxy)-1-(4-[3-{5-methyl-2-pyrid-4-ylloxazol-4-yl}-1-oxoprop-1-yl]-3-fluorophenyl)methylphosphonate;
- 15 Diethyl 1-(hydroxy)-1-(4-[*N*-(2-{5-methyl-2-pyrid-4-ylthiazol-4-yl}ethyl)-*N*-methylaminocarbonyl]-3-fluorophenyl)methylphosphonate;
- Diethyl 1-(hydroxy)-1-(4-[2-{4-(4-trifluoromethylphenyl)phenoxy}ethoxy]-3-fluorophenyl)methylphosphonate;
- Diethyl 1-(hydroxy)-1-(4-[*N*-(2-{4-(4-trifluoromethylphenyl)phenoxy}ethyl)-*N*-
- 20 methylaminocarbonyl]-3-fluorophenyl)methylphosphonate;
- Diethyl 1-(hydroxy)-1-(4-[3-{4-(4-trifluoromethylphenyl)phenoxy}-1-oxoprop-1-yl]-3-fluorophenyl)methylphosphonate;
- Diethyl 1-(hydroxy)-1-(4-[2-{1-[4-(2-trifluoromethylphenyl)phenylmethyl]-3-hexylureido}ethyl]-3-fluorophenyl)methylphosphonate;

- Diethyl 1-(hydroxy)-1-(4-[2-{1-butyl-3-(5-methoxypyrid-2-yl)ureido}ethyl]-3-fluorophenyl)methylphosphonate;
- Diethyl 1-(hydroxy)-1-(4-[3-{4-acetyl-3-hydroxy-2-propylphenoxy}propoxy]-3-fluorophenyl)methylphosphonate;
- 5 Diethyl 1-(hydroxy)-1-(4-[2-{4*H*-3-oxobenzo[1,4]oxazin-2-yl}ethoxy]-3-fluorophenyl)methylphosphonate;
- Diethyl 1-(hydroxy)-1-(4-[3,*N*-phthalimidopropoxy]-3-fluorophenyl)methylphosphonate;
- Diethyl 1-(hydroxy)-1-(4-[4,*N*-phthalimidobutoxy]-3-fluorophenyl)methylphosphonate;
- Tetraethyl 1-(3-[3-{*N*-methyl-*N*-pyrid-2-ylamino}propoxy]-4-fluorophenyl
- 10 )methylidenebisphosphonate;
- Tetraethyl 1-(3-[*N*-(3-{*N*-methyl-*N*-pyrid-2-ylamino}propyl)-*N*-methylamino]-4-fluorophenyl)methylidenebisphosphonate;
- Tetraethyl 1-(3-[3-{*N*-methyl-*N*-pyrid-2-ylamino}-1-oxoprop-1-ylamino]-4-fluorophenyl)methylidenebisphosphonate;
- 15 Tetraethyl 1-(3-[3-{5-methyl-2-phenyloxazol-4-yl}propoxy]-4-fluorophenyl)methylidenebisphosphonate;
- Tetraethyl 1-(3-[*N*-(2-{5-methyl-2-phenyloxazol-4-yl}ethyl)-*N*-methylaminocarbonyl]-4-methoxyphenyl)methylidenebisphosphonate;
- Tetraethyl 1-(3-[3-{5-methyl-2-phenylthiazol-4-yl}propoxy]-4-
- 20 fluorophenyl)methylidenebisphosphonate;
- Tetraethyl 1-(3-[3-{5-methyl-2-phenylthiazol-4-yl}-1-oxoprop-1-yl]-4-fluorophenyl)methylidenebisphosphonate;
- Tetraethyl 1-(3-[4-{5-methyl-2-pyrid-4-ylloxazol-4-yl}butoxy]-4-fluorophenyl)methylidenebisphosphonate;

- Tetraethyl 1-(3-[3-{5-methyl-2-pyrid-4-ylthiazol-4-yl}propoxy]-4-fluorophenyl)methylidenebisphosphonate;
- Tetraethyl 1-(3-[3-{5-methyl-2-pyrid-4-yloxazol-4-yl}-1-oxoprop-1-ylthio]-4-fluorophenyl)methylidenebisphosphonate;
- 5 Tetraethyl 2-(3-[*N*-(3-{5-methyl-2-pyrid-4-ylthiazol-4-yl}propyl)-*N*-methylamino]-4-fluorophenyl)vinylidene-1,1-bisphosphonate;
- Tetraethyl 2-(3-[3-{4-(4-trifluoromethylphenyl)phenoxy}propoxy]-4-fluorophenyl)vinylidene-1,1-bisphosphonate;
- Tetraethyl 2-(3-[*N*-(3-{4-(4-trifluoromethylphenyl)phenoxy}propyl)-*N*-methylamino]-4-
- 10 fluorophenyl)vinylidene-1,1-bisphosphonate;
- Tetraethyl 2-(3-[4-{4-(4-trifluoromethylphenyl)phenoxy}-1-oxobut-1-yl]-4-fluorophenyl)vinylidene-1,1-bisphosphonate;
- Tetraethyl 2-(3-[2-{1-[4-(2-trifluoromethylphenyl)phenylmethyl]-3-hexylureido}ethyl]-4-fluorophenyl)vinylidene-1,1-bisphosphonate;
- 15 Tetraethyl 2-(3-[2-{1-butyl-3-(5-methoxypyrid-2-yl)ureido}ethyl]-4-fluorophenyl)vinylidene-1,1-bisphosphonate;
- Tetraethyl 2-(3-[4-{4-acetyl-3-hydroxy-2-propylphenoxy}butoxy]-4-fluorophenyl)vinylidene-1,1-bisphosphonate;
- Tetraethyl 2-(3-[3-{4*H*-3-oxobenzo[1,4]oxazin-2-yl}propoxy]-4-fluorophenyl)vinylidene-
- 20 1,1-bisphosphonate;
- Tetraethyl 2-(3-[3,*N*-phthalimidopropoxy]-4-fluorophenyl)vinylidene-1,1-bisphosphonate;
- Tetraethyl 2-(3-[4,*N*-phthalimidobutoxy]-4-fluorophenyl)vinylidene-1,1-bisphosphonate;
- Tetraethyl 1-(6-[2-{*N*-methyl-*N*-pyrid-2-ylamino}ethoxy]indol-2-yl)ethylidene-1,2-bisphosphonate;



- Tetraethyl 1-(6-[*N*-(2-{*N*-methyl-*N*-pyrid-2-ylamino} ethyl)-*N*-methylamino]indol-2-yl)ethylidene-1,2-bisphosphonate;
- Tetraethyl 1-(6-[3-{*N*-methyl-*N*-pyrid-2-ylamino}-1-oxoprop-1-yl]indol-2-yl)ethylidene-1,2-bisphosphonate;
- 5 Tetraethyl 1-(6-[2-{5-methyl-2-phenyloxazol-4-yl}ethoxy] indol-2-yl)ethylidene-1,2-bisphosphonate;
- Tetraethyl 1-(6-[*N*-(2-{5-methyl-2-phenyloxazol-4-yl} ethyl)-*N*-methylamino] indol-2-yl)ethylidene-1,2-bisphosphonate;
- Tetraethyl 1-(6-[2-{5-methyl-2-phenylthiazol-4-yl}ethoxy]indol-2-yl)ethylidene-1,2-
- 10 bisphosphonate;
- Tetraethyl 1-(6-[3-{5-methyl-2-phenylthiazol-4-yl}-1-oxoprop-1-yl]indol-2-yl)ethylidene-1,2-bisphosphonate;
- Tetraethyl 1-(6-[2-{5-methyl-2-pyrid-4-yloxazol-4-yl}ethoxy]indol-2-yl)ethylidene-1,2-bisphosphonate;
- 15 Tetraethyl 1-(6-[2-{5-methyl-2-pyrid-4-ylthiazol-4-yl}ethoxy]indol-2-yl)ethylidene-1,2-bisphosphonate;
- Tetraethyl 1-(6-[3-{5-methyl-2-pyrid-4-yloxazol-4-yl}-1-oxoprop-1-yl]indol-2-yl)ethylidene-1,2-bisphosphonate;
- Tetraethyl 2-(6-[*N*-(2-{5-methyl-2-pyrid-4-ylthiazol-4-yl} ethyl)-*N*-methylamino]indol-2-yl)ethylidene-1,1-bisphosphonate;
- 20 Tetraethyl 2-(6-[2-{4-(4-trifluoromethylphenyl)phenoxy}ethoxy] indol-2-yl)ethylidene-1,1-bisphosphonate;
- Tetraethyl 2-(6-[*N*-(2-{4-(4-trifluoromethylphenyl)phenoxy} ethyl)-*N*-methylamino]indol-2-yl)ethylidene-1,1-bisphosphonate;

- Tetraethyl 2-(6-[2-{1-[4-(2-trifluoromethylphenyl)phenylmethyl]-3-hexylureido}ethyl]indol-2-yl)ethylidene-1,1-bisphosphonate;
- Tetraethyl 2-(6-[2-{1-butyl-3-(5-methoxypyrid-2-yl)ureido}ethyl]indol-2-yl)ethylidene-1,1-bisphosphonate;
- 5 Tetraethyl 2-(6-[3-{4-(4-trifluoromethylphenyl)phenoxy}-1-oxoprop-1-yl]indol-2-yl)ethylidene-1,1-bisphosphonate;
- Tetraethyl 2-(6-[3-{4-acetyl-3-hydroxy-2-propylphenoxy}propoxy]indol-2-yl)ethylidene-1,1-bisphosphonate;
- Tetraethyl 2-(6-[2-{4*H*-3-oxobenzo[1,4]oxazin-2-yl}ethoxy]indol-2-yl)ethylidene-1,1-bisphosphonate;
- 10 bisphosphonate;
- Tetraethyl 2-(6-[3,*N*-phthalimidopropoxy]indol-2-yl)ethylidene-1,1-bisphosphonate;
- Tetraethyl 2-(6-[4,*N*-phthalimidobutoxy]indol-2-yl)ethylidene-1,1-bisphosphonate;
- Tetraethyl *N*-(5-[2-{*N*-methyl-*N*-pyrid-2-ylamino}ethoxy]pyrid-2-yl)aminomethylidenebisphosphonate;
- 15 Tetraethyl *N*-(5-[*N*-(2-{*N*-methyl-*N*-pyrid-2-ylamino}ethyl)-*N*-methylamino]pyrid-2-yl)aminomethylidenebisphosphonate;
- Tetraethyl *N*-(5-[3-{*N*-methyl-*N*-pyrid-2-ylamino}-1-oxoprop-1-yl]pyrid-2-yl)aminomethylidenebisphosphonate;
- Tetraethyl *N*-(5-[2-{5-methyl-2-phenyloxazol-4-yl}ethoxy]pyrid-2-yl)aminomethylidenebisphosphonate
- 20 Tetraethyl *N*-(5-[*N*-(2-{5-methyl-2-phenyloxazol-4-yl}ethyl)-*N*-methylamino]pyrid-2-yl)aminomethylidenebisphosphonate;
- Tetraethyl *N*-(5-[2-{5-methyl-2-phenylthiazol-4-yl}ethoxy]pyrid-2-yl)aminomethylidenebisphosphonate;

- Tetraethyl *N*-(5-[3-{5-methyl-2-pyrid-4-yloxazol-4-yl}-1-oxoprop-1-yl]pyrid-2-yl)aminomethylidenebisphosphonate;
- Tetraethyl *N*-(5-[*N*-(2-{5-methyl-2-pyrid-4-ylthiazol-4-yl}ethyl)-*N*-methylamino]pyrid-2-yl)aminomethylidenebisphosphonate;
- 5 Tetraethyl *N*-(5-[2-{5-methyl-2-pyrid-4-yloxazol-4-yl}ethoxy]pyrid-2-yl)aminomethylidenebisphosphonate;
- Tetraethyl *N*-(5-[2-{5-methyl-2-pyrid-4-ylthiazol-4-yl}ethoxy]pyrid-2-yl)aminomethylidenebisphosphonate;
- 2-[1-Hydroxy-1-(5-[*N*-(2-{5-methyl-2-pyrid-4-ylthiazol-4-yl}ethyl)-*N*-
- 10 methylamino]pyrid-2-yl)methyl]-1,3,2-dioxaphospholane-2-oxide;
- 2-[1-Hydroxy-1-(5-[2-{4-(4-trifluoromethylphenyl)phenoxy}ethoxy]-pyrid-2-yl)methyl]-1,3,2-dioxaphospholane-2-oxide;
- 2-[1-Hydroxy-1-(5-[*N*-(2-{4-(4-trifluoromethylphenyl)phenoxy}ethyl)-*N*-methylamino]pyrid-2-yl)methyl]-1,3,2-dioxaphospholane-2-oxide;
- 15 2-[1-Hydroxy-1-(5-[3-{4-(4-trifluoromethylphenyl)phenoxy}-1-oxoprop-1-yl]-pyrid-2-yl)methyl]-1,3,2-dioxaphospholane-2-oxide;
- 2-[1-Hydroxy-1-(5-[2-{1-[4-(2-trifluoromethylphenyl)phenylmethyl]-3-hexylureido}ethyl]pyrid-2-yl)methyl]-1,3,2-dioxaphospholane-2-oxide;
- 2-[1-Hydroxy-1-(5-[2-{1-butyl-3-(5-methoxypyrid-2-yl)ureido}ethyl]pyrid-2-yl)methyl]-1,3,2-dioxaphospholane-2-oxide;
- 20 2-[1-Hydroxy-1-(5-[3-{4-acetyl-3-hydroxy-2-propylphenoxy}propoxy]pyrid-2-yl)methyl]-1,3,2-dioxaphospholane-2-oxide;
- 2-[1-Hydroxy-1-(5-[2-{4*H*-3-oxobenzo[1,4]oxazin-2-yl}ethoxy]pyrid-2-yl)methyl]-1,3,2-dioxaphospholane-2-oxide;

- 2-[1-Hydroxy-1-(5-[3,*N*-phthalimidopropoxy]pyrid-2-yl)methyl]-1,3,2-dioxaphospholane-2-oxide;
- 2-[1-Hydroxy-1-(5-[4,*N*-phthalimidobutoxy]pyrid-2-yl)methyl]-1,3,2-dioxaphospholane-2-oxide;
- 5 2-[1-Hydroxy-1-(5-[2-{*N*-methyl-*N*-pyrid-2-ylamino}ethoxy]benzothien-2-yl)methyl]-[4*R*]-methyl-1,3,2-dioxaphospholane-2-oxide;
- 2-[1-Hydroxy-1-(5-[*N*-(2-{*N*-methyl-*N*-pyrid-2-ylamino}ethyl)-*N*-methylamino]benzothien-2-yl)methyl]-[4*R*]-methyl-1,3,2-dioxaphospholane-2-oxide;
- 2-[1-Hydroxy-1-(5-[3-{*N*-methyl-*N*-pyrid-2-ylamino}-1-oxoprop-1-yl]benzothien-2-yl)methyl]-[4*R*]-methyl-1,3,2-dioxaphospholane-2-oxide;
- 10 2-[1-Hydroxy-1-(5-[2-{5-methyl-2-phenyloxazol-4-yl}ethoxy]benzothien-2-yl)methyl]-[4*R*]-methyl-1,3,2-dioxaphospholane-2-oxide;
- 2-[1-Hydroxy-1-(5-[*N*-(2-{5-methyl-2-phenyloxazol-4-yl}ethyl)-*N*-methylamino]benzothien-2-yl)methyl]-[4*R*]-methyl-1,3,2-dioxaphospholane-2-oxide;
- 15 2-[1-Hydroxy-1-(5-[2-{5-methyl-2-phenylthiazol-4-yl}ethoxy]benzothien-2-yl)methyl]-[4*R*]-methyl-1,3,2-dioxaphospholane-2-oxide;
- 2-[1-Hydroxy-1-(5-[3-{5-methyl-2-phenylthiazol-4-yl}-1-oxoprop-1-yl]benzothien-2-yl)methyl]-[4*R*]-methyl-1,3,2-dioxaphospholane-2-oxide;
- 2-[1-Hydroxy-1-(5-[2-{5-methyl-2-pyrid-4-ylloxazol-4-yl}ethoxy]benzothien-2-yl)methyl]-[4*R*]-methyl-1,3,2-dioxaphospholane-2-oxide;
- 20 2-[1-Hydroxy-1-(5-[2-{5-methyl-2-pyrid-4-ylthiazol-4-yl}ethoxy]benzothien-2-yl)methyl]-[4*R*]-methyl-1,3,2-dioxaphospholane-2-oxide;
- 2-[1-Hydroxy-1-(5-[3-{5-methyl-2-pyrid-4-ylloxazol-4-yl}-1-oxoprop-1-yl]benzothien-2-yl)methyl]-[4*R*]-methyl-1,3,2-dioxaphospholane-2-oxide;

- 2-[1-Hydroxy-1-(5-[*N*-(2-{5-methyl-2-pyrid-4-yl}thiazol-4-yl)ethyl)-*N*-methylamino]benzothien-2-yl)methyl]- [4*S*]-methyl-1,3,2-dioxaphospholane-2-oxide;
- 2-[1-Hydroxy-1-(5-[2-{4-(4-trifluoromethylphenyl)phenoxy}ethoxy]benzothien-2-yl)methyl]- [4*S*]-methyl-1,3,2-dioxaphospholane-2-oxide;
- 5 2-[1-Hydroxy-1-(5-[*N*-(2-{4-(4-trifluoromethylphenyl)phenoxy}ethyl)-*N*-methylamino]benzothien-2-yl)methyl]- [4*S*]-methyl-1,3,2-dioxaphospholane-2-oxide;
- 2-[1-Hydroxy-1-(5-[3-{4-(4-trifluoromethylphenyl)phenoxy}-1-oxoprop-1-yl]benzothien-2-yl)methyl]- [4*S*]-methyl-1,3,2-dioxaphospholane-2-oxide;
- 2-[1-Hydroxy-1-(5-[2-{1-[4-(2-trifluoromethylphenyl)phenylmethyl]-3-hexylureido}ethyl]benzothien-2-yl)methyl]- [4*S*]-methyl-1,3,2-dioxaphospholane-2-oxide;
- 10 2-[1-Hydroxy-1-(5-[2-{1-butyl-3-(5-methoxypyrid-2-yl)ureido}ethyl]benzothien-2-yl)methyl]- [4*S*]-methyl-1,3,2-dioxaphospholane-2-oxide;
- 2-[1-Hydroxy-1-(5-[3-{4-acetyl-3-hydroxy-2-propylphenoxy}propoxy]benzothien-2-yl)methyl]- [4*S*]-methyl-1,3,2-dioxaphospholane-2-oxide;
- 15 2-[1-Hydroxy-1-(5-[2-{4*H*-3-oxobenzo[1,4]oxazin-2-yl}ethoxy]benzothien-2-yl)methyl]- [4*S*]-methyl-1,3,2-dioxaphospholane-2-oxide;
- 2-[1-Hydroxy-1-(5-[3,*N*-phthalimidopropoxy]benzothien-2-yl)methyl]- [4*S*]-methyl-1,3,2-dioxaphospholane-2-oxide;
- 20 2-[1-Hydroxy-1-(5-[4,*N*-phthalimidobutoxy]benzothien-2-yl)methyl]- [4*S*]-methyl-1,3,2-dioxaphospholane-2-oxide;
- 2-[1-Hydroxy-1-(4-[2-{*N*-methyl-*N*-pyrid-2-ylamino}ethoxy]thiazol-2-yl)methyl]-4,5-dimethyl-1,3,2-dioxaphospholane-2-oxide;
- 2-[1-Hydroxy-1-(4-[*N*-(2-{*N*-methyl-*N*-pyrid-2-ylamino}ethyl)-*N*-methylamino]thiazol-2-yl)methyl]-4,5-dimethyl-1,3,2-dioxaphospholane-2-oxide;
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- 2-[1-Hydroxy-1-(4-[3-{*N*-methyl-*N*-pyrid-2-ylamino}-1-oxoprop-1-yl]thiazol-2-yl)methyl]-4,5-dimethyl-1,3,2-dioxaphospholane-2-oxide;
- 2-[1-Hydroxy-1-(4-[2-{5-methyl-2-phenyloxazol-4-yl}ethoxy]thiazol-2-yl)methyl]-4,5-dimethyl-1,3,2-dioxaphospholane-2-oxide;
- 5 2-[1-Hydroxy-1-(4-[*N*-(2-{5-methyl-2-phenyloxazol-4-yl}ethyl)-*N*-methylamino]thiazol-2-yl)methyl]-4,5-dimethyl-1,3,2-dioxaphospholane-2-oxide;
- 2-[1-Hydroxy-1-(4-[2-{5-methyl-2-phenylthiazol-4-yl}ethoxy]thiazol-2-yl)methyl]-4,5-dimethyl-1,3,2-dioxaphospholane-2-oxide;
- 2-[1-Hydroxy-1-(4-[3-{5-methyl-2-phenylthiazol-4-yl}-1-oxoprop-1-yl]thiazol-2-yl)methyl]-4,5-dimethyl-1,3,2-dioxaphospholane-2-oxide;
- 10 2-[1-Hydroxy-1-(4-[2-{5-methyl-2-pyrid-4-yloxazol-4-yl}ethoxy]thiazol-2-yl)methyl]-4,5-dimethyl-1,3,2-dioxaphospholane-2-oxide;
- 2-[1-Hydroxy-1-(4-[2-{5-methyl-2-pyrid-4-ylthiazol-4-yl}ethoxy]thiazol-2-yl)methyl]-4,5-dimethyl-1,3,2-dioxaphospholane-2-oxide;
- 15 2-[1-Hydroxy-1-(4-[3-{5-methyl-2-pyrid-4-yloxazol-4-yl}-1-oxoprop-1-yl]thiazol-2-yl)methyl]-4,5-dimethyl-1,3,2-dioxaphospholane-2-oxide;
- 2-[1-Hydroxy-1-(4-[*N*-(2-{5-methyl-2-pyrid-4-ylthiazol-4-yl}ethyl)-*N*-methylamino]thiazol-2-yl)methyl]-1,3,2-dioxaphosphinane-2-oxide;
- 2-[1-Hydroxy-1-(4-[2-{4-(4-trifluoromethylphenyl)phenoxy}ethoxy]thiazol-2-yl)methyl]-1,3,2-dioxaphosphinane-2-oxide;
- 20 2-[1-Hydroxy-1-(4-[*N*-(2-{4-(4-trifluoromethylphenyl)phenoxy}ethyl)-*N*-methylamino]thiazol-2-yl)methyl]-1,3,2-dioxaphosphinane-2-oxide;
- 2-[1-Hydroxy-1-(4-[3-{4-(4-trifluoromethylphenyl)phenoxy}-1-oxoprop-1-yl]thiazol-2-yl)methyl]-1,3,2-dioxaphosphinane-2-oxide;

- 2-[1-Hydroxy-1-(4-[2-{1-[4-(2-trifluoromethylphenyl)phenylmethyl]-3-hexylureido}ethyl]thiazol-2-yl)methyl]-1,3,2-dioxaphosphinane-2-oxide;
- 2-[1-Hydroxy-1-(4-[2-{1-butyl-3-(5-methoxypyrid-2-yl)ureido}ethyl]thiazol-2-yl)methyl]-1,3,2-dioxaphosphinane-2-oxide;
- 5 2-[1-Hydroxy-1-(4-[3-{4-acetyl-3-hydroxy-2-propylphenoxy}propoxy]thiazol-2-yl)methyl]-1,3,2-dioxaphosphinane-2-oxide;
- 2-[1-Hydroxy-1-(4-[2-{4*H*-3-oxobenzo[1,4]oxazin-2-yl}ethoxy]thiazol-2-yl)methyl]-1,3,2-dioxaphosphinane-2-oxide;
- 2-[1-Hydroxy-1-(4-[3,*N*-phthalimidopropoxy]thiazol-2-yl)methyl]-1,3,2-
- 10 dioxaphosphinane-2-oxide;
- 2-[1-Hydroxy-1-(4-[4,*N*-phthalimidobutoxy]thiazol-2-yl)methyl]-1,3,2-dioxaphosphinane-2-oxide;
- 2[1-(6-[2-{*N*-methyl-*N*-pyrid-2-ylamino}ethoxy]-3-methoxyquinolin-2-yl)-1-(2-oxido-1,3,2-dioxaphospholan-2-yl)methoxy]-1,3,2-dioxaphospholane-2-oxide;
- 15 2[1-(6-[*N*-(2-{*N*-methyl-*N*-pyrid-2-ylamino}ethyl)-*N*-methylamino]-3-methoxyquinolin-2-yl)-1-(2-oxido-1,3,2-dioxaphospholan-2-yl)methoxy]-1,3,2-dioxaphospholane-2-oxide;
- 2[1-(6-[3-{*N*-methyl-*N*-pyrid-2-ylamino}-1-oxoprop-1-yl]-3-methoxyquinolin-2-yl)-1-(2-oxido-1,3,2-dioxaphospholan-2-yl)methoxy]-1,3,2-dioxaphospholane-2-oxide;
- 20 2[1-(6-[2-{5-methyl-2-phenyloxazol-4-yl}ethoxy]-3-methoxyquinolin-2-yl)-1-(2-oxido-1,3,2-dioxaphospholan-2-yl)methoxy]-1,3,2-dioxaphospholane-2-oxide;
- 2[1-(6-[*N*-(2-{5-methyl-2-phenyloxazol-4-yl}ethyl)-*N*-methylamino]-3-methoxyquinolin-2-yl)-1-(2-oxido-1,3,2-dioxaphospholan-2-yl)methoxy]-1,3,2-dioxaphospholane-2-oxide;

- 2[1-(6-[2-{5-methyl-2-phenylthiazol-4-yl}ethoxy]-3-methoxyquinolin-2-yl)-1-(2-oxido-1,3,2-dioxaphospholan-2-yl)methoxy]-1,3,2-dioxaphospholane-2-oxide;
- 2[1-(6-[3-{5-methyl-2-phenylthiazol-4-yl}-1-oxoprop-1-yl]-3-methoxyquinolin-2-yl)-1-(2-oxido-1,3,2-dioxaphospholan-2-yl)methoxy]-1,3,2-dioxaphospholane-2-oxide;
- 5 2[1-(6-[2-{5-methyl-2-pyrid-4-yloxazol-4-yl}ethoxy]-3-methoxyquinolin-2-yl)-1-(2-oxido-1,3,2-dioxaphospholan-2-yl)methoxy]-1,3,2-dioxaphospholane-2-oxide;
- 2[1-(6-[2-{5-methyl-2-pyrid-4-ylthiazol-4-yl}ethoxy]-3-methoxyquinolin-2-yl)-1-(2-oxido-1,3,2-dioxaphospholan-2-yl)methoxy]-1,3,2-dioxaphospholane-2-oxide;
- 2[1-(6-[3-{5-methyl-2-pyrid-4-yloxazol-4-yl}-1-oxoprop-1-yl]-3-methoxyquinolin-2-yl)-1-(2-oxido-1,3,2-dioxaphospholan-2-yl)methoxy]-1,3,2-dioxaphospholane-2-oxide;
- 10 2[1-(6-[*N*-(2-{5-methyl-2-pyrid-4-ylthiazol-4-yl}ethyl)-*N*-methylamino]-3-methoxyquinolin-2-yl)-1-([4*R*]-methyl-2-oxido-1,3,2-dioxaphospholan-2-yl)methoxy]-[4*R*]-methyl-1,3,2-dioxaphospholane-2-oxide;
- 2[1-(6-[2-{4-(4-trifluoromethylphenyl)phenoxy}ethoxy]-3-methoxyquinolin-2-yl)-1-([4*R*]-methyl-2-oxido-1,3,2-dioxaphospholan-2-yl)methoxy]-[4*R*]-methyl-1,3,2-dioxaphospholane-2-oxide;
- 15 2[1-(6-[*N*-(2-{4-(4-trifluoromethylphenyl)phenoxy}ethyl)-*N*-methylamino]-3-methoxyquinolin-2-yl)-1-([4*R*]-methyl-2-oxido-1,3,2-dioxaphospholan-2-yl)methoxy]-[4*R*]-methyl-1,3,2-dioxaphospholane-2-oxide;
- 20 2[1-(6-[3-{4-(4-trifluoromethylphenyl)phenoxy}-1-oxoprop-1-yl]-3-methoxyquinolin-2-yl)-1-([4*R*]-methyl-2-oxido-1,3,2-dioxaphospholan-2-yl)methoxy]-[4*R*]-methyl-1,3,2-dioxaphospholane-2-oxide;
- 2[1-(6-[2-{1-[4-(2-trifluoromethylphenyl)phenylmethyl]-3-hexylureido}ethyl]-3-methoxyquinolin-2-yl)-1-([4*R*]-methyl-2-oxido-1,3,2-dioxaphospholan-2-yl)methoxy]-[4*R*]-methyl-1,3,2-dioxaphospholane-2-oxide;
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- 2[1-(6-[2-{1-butyl-3-(5-methoxypyrid-2-yl)ureido}ethyl]-3-methoxyquinolin-2-yl)-1-  
 ([4R]-methyl-2-oxido-1,3,2-dioxaphospholan-2-yl)methoxy]-[4R]-methyl-1,3,2-  
 dioxaphospholane-2-oxide;
- 2[1-(6-[3-{4-acetyl-3-hydroxy-2-propylphenoxy}propoxy]-3-methoxyquinolin-2-yl)-1-  
 5 ([4R]-methyl-2-oxido-1,3,2-dioxaphospholan-2-yl)methoxy]-[4R]-methyl-1,3,2-  
 dioxaphospholane-2-oxide;
- 2[1-(6-[2-{4*H*-3-oxobenzo[1,4]oxazin-2-yl}ethoxy]-3-methoxyquinolin-2-yl)-1-([4R]-  
 methyl-2-oxido-1,3,2-dioxaphospholan-2-yl)methoxy]-[4R]-methyl-1,3,2-  
 dioxaphospholane-2-oxide;
- 10 2[1-(6-[3-*N*-phthalimidopropoxy]-3-methoxyquinolin-2-yl)-1-([4R]-methyl-2-oxido-1,3,2-  
 dioxaphospholan-2-yl)methoxy]-[4R]-methyl-1,3,2-dioxaphospholane-2-oxide;
- 2[1-(6-[4-*N*-phthalimidobutoxy]-3-methoxyquinolin-2-yl)-1-([4R]-methyl-2-oxido-1,3,2-  
 dioxaphospholan-2-yl)methoxy]-[4R]-methyl-1,3,2-dioxaphospholane-2-oxide;
- 2[1-(5-[2-{*N*-methyl-*N*-pyrid-2-ylamino}ethoxy]thien-2-yl)-1-([4S]-methyl-2-oxido-  
 15 1,3,2-dioxaphospholan-2-yl)methoxy]- [4S]-methyl-1,3,2-dioxaphospholane-2-oxide;
- 2[1-(5-[*N*-(2-{*N*-methyl-*N*-pyrid-2-ylamino}ethyl)-*N*-methylanino]thien-2-yl)-1-([4S]-  
 methyl-2-oxido-1,3,2-dioxaphospholan-2-yl)methoxy]- [4S]-methyl-1,3,2-  
 dioxaphospholane-2-oxide;
- 2[1-(5-[3-{*N*-methyl-*N*-pyrid-2-ylamino}-1-oxoprop-1-yl]thien-2-yl)-1-([4S]-methyl-2-  
 20 oxido-1,3,2-dioxaphospholan-2-yl)methoxy]- [4S]-methyl-1,3,2-dioxaphospholane-2-  
 oxide;
- 2[1-(5-[2-{5-methyl-2-phenyloxazol-4-yl}ethoxy]thien-2-yl)-1-([4S]-methyl-2-oxido-  
 1,3,2-dioxaphospholan-2-yl)methoxy]- [4S]-methyl-1,3,2-dioxaphospholane-2-oxide;

- 2[1-(5-[*N*-(2-{5-methyl-2-phenyloxazol-4-yl}ethyl)-*N*-methylamino]thien-2-yl)-1-([4*S*]-methyl-2-oxido-1,3,2-dioxaphospholan-2-yl)methoxy]- [4*S*]-methyl-1,3,2-dioxaphospholane-2-oxide;
- 2[1-(5-[2-{5-methyl-2-phenylthiazol-4-yl}ethoxy]thien-2-yl)-1-([4*S*]-methyl-2-oxido-1,3,2-dioxaphospholan-2-yl)methoxy]- [4*S*]-methyl-1,3,2-dioxaphospholane-2-oxide;
- 5 2[1-(5-[3-{5-methyl-2-phenylthiazol-4-yl}-1-oxoprop-1-yl]thien-2-yl)-1-([4*S*]-methyl-2-oxido-1,3,2-dioxaphospholan-2-yl)methoxy]- [4*S*]-methyl-1,3,2-dioxaphospholane-2-oxide;
- 2[1-(5-[2-{5-methyl-2-pyrid-4-yloxazol-4-yl}ethoxy]thien-2-yl)-1-([4*S*]-methyl-2-oxido-1,3,2-dioxaphospholan-2-yl)methoxy]- [4*S*]-methyl-1,3,2-dioxaphospholane-2-oxide;
- 10 2[1-(5-[2-{5-methyl-2-pyrid-4-ylthiazol-4-yl}ethoxy]thien-2-yl)-1-([4*S*]-methyl-2-oxido-1,3,2-dioxaphospholan-2-yl)methoxy]- [4*S*]-methyl-1,3,2-dioxaphospholane-2-oxide;
- 2[1-(5-[3-{5-methyl-2-pyrid-4-yloxazol-4-yl}-1-oxoprop-1-yl]thien-2-yl)-1-([4*S*]-methyl-2-oxido-1,3,2-dioxaphospholan-2-yl)methoxy]- [4*S*]-methyl-1,3,2-dioxaphospholane-2-oxide;
- 15 2[1-(5-[*N*-(2-{5-methyl-2-pyrid-4-ylthiazol-4-yl}ethyl)-*N*-methylamino]thien-2-yl)-1-(4,5-dimethyl-2-oxido-1,3,2-dioxaphospholan-2-yl)methoxy]-4,5-dimethyl-1,3,2-dioxaphospholane-2-oxide;
- 2[1-(5-[2-{4-(4-trifluoromethylphenyl)phenoxy}ethoxy]thien-2-yl)-1-(4,5-dimethyl-2-oxido-1,3,2-dioxaphospholan-2-yl)methoxy]-4,5-dimethyl-1,3,2-dioxaphospholane-2-oxide;
- 20 2[1-(5-[*N*-(2-{4-(4-trifluoromethylphenyl)phenoxy}ethyl)-*N*-methylamino]thien-2-yl)-1-(4,5-dimethyl-2-oxido-1,3,2-dioxaphospholan-2-yl)methoxy]-4,5-dimethyl-1,3,2-dioxaphospholane-2-oxide;

- 2[1-(5-[3-{4-(4-trifluoromethylphenyl)phenoxy}-1-oxoprop-1-yl]thien-2-yl)-1-(4,5-dimethyl-2-oxido-1,3,2-dioxaphospholan-2-yl)methoxy]-4,5-dimethyl-1,3,2-dioxaphospholane-2-oxide;
- 2[1-(5-[2-{1-[4-(2-trifluoromethylphenyl)phenylmethyl]-3-hexylureido}ethyl]thien-2-yl)-1-(4,5-dimethyl-2-oxido-1,3,2-dioxaphospholan-2-yl)methoxy]-4,5-dimethyl-1,3,2-dioxaphospholane-2-oxide;
- 2[1-(5-[2-{1-butyl-3-(5-methoxypyrid-2-yl)ureido}ethyl]thien-2-yl)-1-(4,5-dimethyl-2-oxido-1,3,2-dioxaphospholan-2-yl)methoxy]-4,5-dimethyl-1,3,2-dioxaphospholane-2-oxide;
- 2[1-(5-[3-{4-acetyl-3-hydroxy-2-propylphenoxy}propoxy]thien-2-yl)-1-(4,5-dimethyl-2-oxido-1,3,2-dioxaphospholan-2-yl)methoxy]-4,5-dimethyl-1,3,2-dioxaphospholane-2-oxide;
- 2[1-(5-[2-{4*H*-3-oxobenzo[1,4]oxazin-2-yl}ethoxy]thien-2-yl)-1-(4,5-dimethyl-2-oxido-1,3,2-dioxaphospholan-2-yl)methoxy]-4,5-dimethyl-1,3,2-dioxaphospholane-2-oxide;
- 2[1-(5-[3-*N*-phthalimidopropoxy]thien-2-yl)-1-(4,5-dimethyl-2-oxido-1,3,2-dioxaphospholan-2-yl)methoxy]-4,5-dimethyl-1,3,2-dioxaphospholane-2-oxide;
- 2[1-(5-[4-*N*-phthalimidobutoxy]thien-2-yl)-1-(4,5-dimethyl-2-oxido-1,3,2-dioxaphospholan-2-yl)methoxy]-4,5-dimethyl-1,3,2-dioxaphospholane-2-oxide;
- 2[1-(4-[2-{*N*-methyl-*N*-pyrid-2-ylamino}ethoxy]-3-fluorophenyl)-1-(2-oxido-1,3,2-dioxaphosphinan-2-yl)methoxy]-1,3,2-dioxaphosphinane-2-oxide;
- 2[1-(4-[*N*-(2-{*N*-methyl-*N*-pyrid-2-ylamino}ethyl)-*N*-methylaminocarbonyl]-3-fluorophenyl)-1-(2-oxido-1,3,2-dioxaphosphinan-2-yl)methoxy]-1,3,2-dioxaphosphinane-2-oxide;
- 2[1-(4-[3-{*N*-methyl-*N*-pyrid-2-ylamino}-1-oxoprop-1-yl]-3-fluorophenyl)-1-(2-oxido-1,3,2-dioxaphosphinan-2-yl)methoxy]-1,3,2-dioxaphosphinane-2-oxide;

- 2[1-(4-[2-{5-methyl-2-phenyloxazol-4-yl}ethoxy]-3-fluorophenyl)-1-(2-oxido-1,3,2-dioxaphosphinan-2-yl)methoxy]-1,3,2-dioxaphosphinane-2-oxide;
- 1-(4-[*N*-(2-{5-methyl-2-phenyloxazol-4-yl}ethyl)-*N*-methylaminocarbonyl]-3-fluorophenyl)-1,1-bis(2-oxido-1,3,2-dioxaphospholan-2-yl)methane;
- 5 1-(4-[2-{5-methyl-2-phenylthiazol-4-yl}ethoxy]-3-fluorophenyl)-1,1-bis(2-oxido-1,3,2-dioxaphospholan-2-yl)methane;
- 1-(4-[3-{5-methyl-2-phenylthiazol-4-yl}-1-oxoprop-1-yl]-3-fluorophenyl)-1,1-bis(2-oxido-1,3,2-dioxaphospholan-2-yl)methane;
- 1-(4-[2-{5-methyl-2-pyrid-4-yloxazol-4-yl}ethoxy]-3-fluorophenyl)-1,1-bis(2-oxido-1,3,2-dioxaphospholan-2-yl)methane;
- 10 1-(4-[2-{5-methyl-2-pyrid-4-ylthiazol-4-yl}ethoxy]-3-fluorophenyl)-1,1-bis(4,5-dimethyl-2-oxido-1,3,2-dioxaphospholan-2-yl)methane;
- 1-(4-[3-{5-methyl-2-pyrid-4-yloxazol-4-yl}-1-oxoprop-1-yl]-3-fluorophenyl)-1,1-bis(2-oxido-1,3,2-dioxaphosphinan-2-yl)methane;
- 15 1-(4-[*N*-(2-{5-methyl-2-pyrid-4-ylthiazol-4-yl}ethyl)-*N*-methylaminocarbonyl]-3-fluorophenyl)-1,1-bis(4,5-dimethyl-2-oxido-1,3,2-dioxaphospholan-2-yl)methane;
- 1-(4-[2-{4-(4-trifluoromethylphenyl)phenoxy}ethoxy]-3-fluorophenyl)-1,1-bis(2-oxido-1,3,2-dioxaphosphinan-2-yl)methane;
- 1-(4-[*N*-(2-{4-(4-trifluoromethylphenyl)phenoxy}ethyl)-*N*-methylaminocarbonyl]-3-fluorophenyl)-1,1-bis(4,5-dimethyl-2-oxido-1,3,2-dioxaphospholan-2-yl)methane;
- 20 1-(4-[3-{4-(4-trifluoromethylphenyl)phenoxy}-1-oxoprop-1-yl]-3-fluorophenyl)-1,1-bis(2-oxido-1,3,2-dioxaphosphinan-2-yl)methane;
- 1-(4-[2-{1-[4-(2-trifluoromethylphenyl)phenylmethyl]-3-hexylureido}ethyl]-3-fluorophenyl)-1,1-bis(4,5-dimethyl-2-oxido-1,3,2-dioxaphospholan-2-yl)methane;

- 1-(4-[2-{1-butyl-3-(5-methoxypyrid-2-yl)ureido}ethyl]-3-fluorophenyl)-1,1-bis(2-oxido-1,3,2-dioxaphosphinan-2-yl)methane;
- 2-(4-[3-{4-acetyl-3-hydroxy-2-propylphenoxy}propoxy]-3-fluorophenyl)-1,2-bis(2-oxido-1,3,2-dioxaphospholan-2-yl)ethane;
- 5 2-(4-[2-{4*H*-3-oxobenzo[1,4]oxazin-2-yl}ethoxy]-3-fluorophenyl)-1,2-bis([4*R*]-methyl-2-oxido-1,3,2-dioxaphospholan-2-yl)ethane;
- 2-(4-[3,*N*-phthalimidopropoxy]-3-fluorophenyl)-1,2-bis(2-oxido-1,3,2-dioxaphospholan-2-yl)ethane;
- 2-(4-[4,*N*-phthalimidobutoxy]-3-fluorophenyl)-1,2-bis([4*R*]-methyl-2-oxido-1,3,2-dioxaphospholan-2-yl)ethane;
- 10 2-(3-[3-{*N*-methyl-*N*-pyrid-2-ylamino}propoxy]-4-fluorophenyl)-1,2-bis(2-oxido-1,3,2-dioxaphospholan-2-yl)ethane;
- 2-(3-[*N*-(3-{*N*-methyl-*N*-pyrid-2-ylamino}propyl)-*N*-methylanino]-4-fluorophenyl)-1,2-bis([4*R*]-methyl-2-oxido-1,3,2-dioxaphospholan-2-yl)ethane;
- 15 2-(3-[3-{*N*-methyl-*N*-pyrid-2-ylamino}-1-oxoprop-1-ylamino]-4-fluorophenyl)-1,2-bis(2-oxido-1,3,2-dioxaphospholan-2-yl)ethane;
- 2-(3-[3-{5-methyl-2-phenyloxazol-4-yl}propoxy]-4-fluorophenyl)-1,2-bis([4*R*]-methyl-2-oxido-1,3,2-dioxaphospholan-2-yl)ethane;
- 2-(3-[*N*-(2-{5-methyl-2-phenyloxazol-4-yl}ethyl)-*N*-methyaminocarbonyl]-4-methoxyphenyl)-1,1-bis(4,5-dimethyl-2-oxido-1,3,2-dioxaphospholan-2-yl)ethane;
- 20 2-(3-[3-{5-methyl-2-phenylthiazol-4-yl}propoxy]-4-fluorophenyl)-1,1-bis(2-oxido-1,3,2-dioxaphosphinan-2-yl)ethane;
- 2-(3-[3-{5-methyl-2-phenylthiazol-4-yl}-1-oxoprop-1-yl]-4-fluorophenyl)-1,1-bis(4,5-dimethyl-2-oxido-1,3,2-dioxaphospholan-2-yl)ethane;

- 2-(3-[4-{5-methyl-2-pyrid-4-yloxazol-4-yl}butoxy]-4-fluorophenyl)-1,1-bis(2-oxido-1,3,2-dioxaphosphinan-2-yl)ethane;
- 2-(3-[3-{5-methyl-2-pyrid-4-ylthiazol-4-yl}propoxy]-4-fluorophenyl)-1,1-bis(4,5-dimethyl-2-oxido-1,3,2-dioxaphospholan-2-yl)ethane;
- 5 2-(3-[3-{5-methyl-2-pyrid-4-yloxazol-4-yl}-1-oxoprop-1-ylthio]-4-fluorophenyl)-1,1-bis(2-oxido-1,3,2-dioxaphosphinan-2-yl)ethane;
- 2-(3-[*N*-(3-{5-methyl-2-pyrid-4-ylthiazol-4-yl}propyl)-*N*-methylamino]-4-fluorophenyl)-1,1-bis(4,5-dimethyl-2-oxido-1,3,2-dioxaphospholan-2-yl)ethane;
- 2-(3-[3-{4-(4-trifluoromethylphenyl)phenoxy}propoxy]-4-fluorophenyl)-1,1-bis(2-oxido-1,3,2-dioxaphosphinan-2-yl)ethane;
- 10 1-[*N*-(3-[*N*-(3-{4-(4-trifluoromethylphenyl)phenoxy}propyl)-*N*-methylamino]-4-fluorophenyl)amino]-1,1-bis(2-oxido-1,3,2-dioxaphospholan-2-yl)methane;
- 1-[*N*-(3-[4-{4-(4-trifluoromethylphenyl)phenoxy}-1-oxobut-1-yl]-4-fluorophenyl)amino]-1,1-bis([4*R*]-methyl-2-oxido-1,3,2-dioxaphospholan-2-yl)methane;
- 15 1-[*N*-(3-[2-{1-[4-(2-trifluoromethylphenyl)phenylmethyl]-3-hexylureido}ethyl]-4-fluorophenyl)amino]-1,1-bis(2-oxido-1,3,2-dioxaphospholan-2-yl)methane;
- 1-[*N*-(3-[2-{1-butyl-3-(5-methoxypyrid-2-yl)ureido}ethyl]-4-fluorophenyl)amino]-1,1-bis([4*R*]-methyl-2-oxido-1,3,2-dioxaphospholan-2-yl)methane;
- 1-[*N*-(3-[4-{4-acetyl-3-hydroxy-2-propylphenoxy}butoxy]-4-fluorophenyl)amino]-1,1-bis(2-oxido-1,3,2-dioxaphospholan-2-yl)methane;
- 20 1-[*N*-(3-[3-{4*H*-3-oxobenzo[1,4]oxazin-2-yl}propoxy]-4-fluorophenyl)amino]-1,1-bis([4*R*]-methyl-2-oxido-1,3,2-dioxaphospholan-2-yl)methane;
- 1-[*N*-(3-[3,*N*-phthalimidopropoxy]-4-fluorophenyl)amino]-1,1-bis(2-oxido-1,3,2-dioxaphospholan-2-yl)methane;

- 1-[*N*-(3-[4,*N*-phthalimidobutoxy]-4-fluorophenyl)amino]-1,1-bis([4*R*]-methyl-2-oxido-1,3,2-dioxaphospholan-2-yl)methane;
- 1-[*N*-(6-[2-{*N*-methyl-*N*-pyrid-2-ylamino}ethoxy]indol-2-yl)amino]-1,1-bis(2-oxido-1,3,2-dioxaphosphinan-2-yl)methane;
- 5 1-[*N*-(6-[*N*-(2-{*N*-methyl-*N*-pyrid-2-ylamino}ethyl)-*N*-methylamino]indol-2-yl)amino]-1,1-bis(2-oxido-1,3,2-dioxaphosphinan-2-yl)methane;
- 1-[*N*-(6-[3-{*N*-methyl-*N*-pyrid-2-ylamino}-1-oxoprop-1-yl]indol-2-yl)amino]-1,1-bis(2-oxido-1,3,2-dioxaphosphinan-2-yl)methane;
- 1-[*N*-(6-[2-{5-methyl-2-phenyloxazol-4-yl}ethoxy] indol-2-yl)amino]-1,1-bis(2-oxido-1,3,2-dioxaphosphinan-2-yl)methane;
- 10 2-[1-(Diethoxyphosphinyloxy)-1-(6-[*N*-(2-{5-methyl-2-phenyloxazol-4-yl}ethyl)-*N*-methylamino] indol-2-yl)methyl]-1,3,2-dioxaphospholane-2-oxide;
- 2-[1-(Diethoxyphosphinyloxy)-1-(6-[2-{5-methyl-2-phenylthiazol-4-yl}ethoxy]indol-2-yl)methyl]-1,3,2-dioxaphospholane-2-oxide;
- 15 2-[1-(Diethoxyphosphinyloxy)-1-(6-[3-{5-methyl-2-phenylthiazol-4-yl}-1-oxoprop-1-yl]indol-2-yl)methyl]-1,3,2-dioxaphospholane-2-oxide;
- 2-[1-(Diethoxyphosphinyloxy)-1-(6-[2-{5-methyl-2-pyrid-4-yloxazol-4-yl}ethoxy]indol-2-yl)methyl]-1,3,2-dioxaphospholane-2-oxide;
- 2-[1-(Diethoxyphosphinyloxy)-1-(6-[2-{5-methyl-2-pyrid-4-ylthiazol-4-yl}ethoxy]indol-2-yl)methyl]-1,3,2-dioxaphosphinane-2-oxide;
- 20 2-[1-(Diethoxyphosphinyloxy)-1-(6-[3-{5-methyl-2-pyrid-4-yloxazol-4-yl}-1-oxoprop-1-yl]indol-2-yl)methyl]-1,3,2-dioxaphosphinane-2-oxide;
- 2-[1-(Diethoxyphosphinyloxy)-1-(6-[*N*-(2-{5-methyl-2-pyrid-4-ylthiazol-4-yl}ethyl)-*N*-methylamino]indol-2-yl)methyl]-1,3,2-dioxaphosphinane-2-oxide;

- 2-[1-(Diethoxyphosphinyloxy)-1-(6-[2-{4-(4-trifluoromethylphenyl)phenoxy}ethoxy]indol-2-yl)methyl]-1,3,2-dioxaphosphinane-2-oxide;
- 2[1-(6-[*N*-(2-{4-(4-trifluoromethylphenyl)phenoxy}ethyl)-*N*-methylamino]indol-2-yl)-1-(diethoxyphosphinyl)methoxy]-4[S]-methyl-1,3,2-dioxaphospholane-2-oxide;
- 5 2[1-(6-[3-{4-(4-trifluoromethylphenyl)phenoxy}-1-oxoprop-1-yl]indol-2-yl)-1-(diethoxyphosphinyl)methoxy]-4,5-dimethyl-1,3,2-dioxaphospholane-2-oxide;
- 2[1-(6-[2-{1-[4-(2-trifluoromethylphenyl)phenylmethyl]-3-hexylureido}ethyl]indol-2-yl)-1-(diethoxyphosphinyl)methoxy]-4[S]-methyl-1,3,2-dioxaphospholane-2-oxide;
- 2[1-(6-[2-{1-[4-(2-trifluoromethylphenyl)phenylmethyl]-3-hexylureido}ethyl]indol-2-yl)-1-(diethoxyphosphinyl)methoxy]-4,5-dimethyl-1,3,2-dioxaphospholane-2-oxide;
- 10 2[1-(6-[3-{4-acetyl-3-hydroxy-2-propylphenoxy}propoxy]indol-2-yl)-1-(diethoxyphosphinyl)methoxy]-4[S]-methyl-1,3,2-dioxaphospholane-2-oxide;
- 2[1-(6-[2-{4*H*-3-oxobenzo[1,4]oxazin-2-yl}ethoxy]indol-2-yl)-1-(diethoxyphosphinyl)methoxy]-4,5-dimethyl-1,3,2-dioxaphospholane-2-oxide;
- 15 2[1-(6-[2-{1-butyl-3-(5-methoxypyrid-2-yl)ureido}ethyl]indol-2-yl)-1-(diethoxyphosphinyl)methoxy]-4[S]-methyl-1,3,2-dioxaphospholane-2-oxide;
- 2[1-(6-[3,*N*-phthalimidopropoxy]indol-2-yl)-1-(diethoxyphosphinyl)methoxy]-4,5-dimethyl-1,3,2-dioxaphospholane-2-oxide;
- 2[1-(6-[4,*N*-phthalimidobutoxy]indol-2-yl)-1-(diethoxyphosphinyl)methyl]-4[R]-methyl-1,3,2-dioxaphospholane-2-oxide;
- 20 2[1-(5-[2-{*N*-methyl-*N*-pyrid-2-ylamino}ethoxy]pyrid-2-yl)-1-(diethoxyphosphinyl)methyl]-4[R]-methyl-1,3,2-dioxaphospholane-2-oxide;
- 2[1-(5-[*N*-(2-{*N*-methyl-*N*-pyrid-2-ylamino}ethyl)-*N*-methylamino]pyrid-2-yl)-1-(diethoxyphosphinyl)methyl]-4[R]-methyl-1,3,2-dioxaphospholane-2-oxide;



- 2[1-(5-[3-{*N*-methyl-*N*-pyrid-2-ylamino}-1-oxoprop-1-yl]pyrid-2-yl)-1-(diethoxyphosphinyl)methyl]-4[R]-methyl-1,3,2-dioxaphospholane-2-oxide;
- 2[1-(5-[2-{5-methyl-2-phenyloxazol-4-yl}ethoxy]pyrid-2-yl)-1-(diethoxyphosphinyl)methyl]-1,3,2-dioxaphosphinane-2-oxide;
- 5 2[1-(5-[*N*-(2-{5-methyl-2-phenyloxazol-4-yl}ethyl)-*N*-methylamino]pyrid-2-yl)-1-(diethoxyphosphinyl)methyl]-1,3,2-dioxaphosphinane-2-oxide;
- 2[1-(5-[*N*-(2-{5-methyl-2-phenyloxazol-4-yl}ethyl)-*N*-methylamino]pyrid-2-yl)-1-(diethoxyphosphinyl)methyl]-1,3,2-dioxaphosphinane-2-oxide;
- 2[1-(5-[2-{5-methyl-2-phenylthiazol-4-yl}ethoxy]pyrid-2-yl)-1-(diethoxyphosphinyl)methyl]-1,3,2-dioxaphosphinane-2-oxide;
- 10 2[1-(5-[3-{5-methyl-2-phenylthiazol-4-yl}-1-oxoprop-1-yl]pyrid-2-yl)-2-(diethoxyphosphinyl)eth-1-yl]-4,5-dimethyl-1,3,2-dioxaphospholane-2-oxide;
- 2[1-(5-[2-{5-methyl-2-pyrid-4-yloxazol-4-yl}ethoxy]pyrid-2-yl)-2-(diethoxyphosphinyl)eth-1-yl]-1,3,2-dioxaphosphinane-2-oxide;
- 15 2[1-(5-[2-{5-methyl-2-pyrid-4-ylthiazol-4-yl}ethoxy]pyrid-2-yl)-2-(diethoxyphosphinyl)eth-1-yl]-4,5-dimethyl-1,3,2-dioxaphospholane-2-oxide;
- 2[1-(5-[3-{5-methyl-2-pyrid-4-yloxazol-4-yl}-1-oxoprop-1-yl]pyrid-2-yl)-2-(diethoxyphosphinyl)eth-1-yl]-1,3,2-dioxaphosphinane-2-oxide;
- 2[1-(5-[*N*-(2-{5-methyl-2-pyrid-4-ylthiazol-4-yl}ethyl)-*N*-methylamino]pyrid-2-yl)-2-(diethoxyphosphinyl)eth-1-yl]-4,5-dimethyl-1,3,2-dioxaphospholane-2-oxide;
- 20 2[1-(5-[2-{4-(4-trifluoromethylphenyl)phenoxy}ethoxy]-pyrid-2-yl)-2-(diethoxyphosphinyl)eth-1-yl]-1,3,2-dioxaphosphinane-2-oxide;
- 2[1-(5-[*N*-(2-{4-(4-trifluoromethylphenyl)phenoxy}ethyl)-*N*-methylamino]pyrid-2-yl)-2-(diethoxyphosphinyl)eth-1-yl]-4,5-dimethyl-1,3,2-dioxaphospholane-2-oxide;

- 2[1-(5-[3-{4-(4-trifluoromethylphenyl)phenoxy}-1-oxoprop-1-yl]-pyrid-2-yl)-2-(diethoxyphosphinyl)eth-1-yl]-1,3,2-dioxaphosphinane-2-oxide;
- 2[2-(5-[2-{1-[4-(2-trifluoromethylphenyl)phenylmethyl]-3-hexylureido}ethyl]pyrid-2-yl)-2-(diethoxyphosphinyl)eth-1-yl]-1,3,2-dioxaphospholane-2-oxide;
- 5 2[2-(5-[2-{1-butyl-3-(5-methoxypyrid-2-yl)ureido}ethyl]pyrid-2-yl)-2-(diethoxyphosphinyl)eth-1-yl]-4[R]-methyl-1,3,2-dioxaphospholane-2-oxide;
- 2[2-(5-[3-{4-acetyl-3-hydroxy-2-propylphenoxy}propoxy]pyrid-2-yl)-2-(diethoxyphosphinyl)eth-1-yl]-1,3,2-dioxaphospholane-2-oxide;
- 2[2-(5-[2-{4*H*-3-oxobenzo[1,4]oxazin-2-yl}ethoxy]pyrid-2-yl)-2-(diethoxyphosphinyl)eth-1-yl]-4[R]-methyl-1,3,2-dioxaphospholane-2-oxide;
- 10 2[2-(5-[3,*N*-phthalimidopropoxy]pyrid-2-yl)-2-(diethoxyphosphinyl)eth-1-yl]-1,3,2-dioxaphospholane-2-oxide;
- 2[2-(5-[4,*N*-phthalimidobutoxy]pyrid-2-yl)-2-(diethoxyphosphinyl)eth-1-yl]-4[R]-methyl-1,3,2-dioxaphospholane-2-oxide;
- 15 2[2-(5-[2-{*N*-methyl-*N*-pyrid-2-ylamino}ethoxy]benzothien-2-yl)-2-(diethoxyphosphinyl)eth-1-yl]-1,3,2-dioxaphospholane-2-oxide;
- 2[2-(5-[*N*-(2-{*N*-methyl-*N*-pyrid-2-ylamino}ethyl)-*N*-methylanino]benzothien-2-yl)-2-(diethoxyphosphinyl)eth-1-yl]-4[R]-methyl-1,3,2-dioxaphospholane-2-oxide;
- 2[2-(5-[3-{*N*-methyl-*N*-pyrid-2-ylamino}-1-oxoprop-1-yl]benzothien-2-yl)-2-(diethoxyphosphinyl)eth-1-yl]-1,3,2-dioxaphosphinane-2-oxide;
- 20 2[2-(5-[2-{5-methyl-2-phenyloxazol-4-yl}ethoxy]benzothien-2-yl)-2-(diethoxyphosphinyl)eth-1-yl]-1,3,2-dioxaphosphinane-2-oxide;
- 2[2-(5-[*N*-(2-{5-methyl-2-phenyloxazol-4-yl}ethyl)-*N*-methylanino]benzothien-2-yl)-2-(diethoxyphosphinyl)eth-1-yl]-1,3,2-dioxaphosphinane-2-oxide;

- 2[2-(5-[2-{5-methyl-2-phenylthiazol-4-yl}ethoxy]benzothien-2-yl)-2-(diethoxyphosphinyl)eth-1-yl]-1,3,2-dioxaphosphinane-2-oxide;
- 2[2-(5-[3-{5-methyl-2-phenylthiazol-4-yl}-1-oxoprop-1-yl]benzothien-2-yl)-1-(diethoxyphosphinyl)eth-1-yl]-1,3,2-dioxaphospholane-2-oxide;
- 5 2[2-(5-[2-{5-methyl-2-pyrid-4-yloxazol-4-yl}ethoxy]benzothien-2-yl)-1-(diethoxyphosphinyl)eth-1-yl]-1,3,2-dioxaphospholane-2-oxide;
- 2[2-(5-[2-{5-methyl-2-pyrid-4-ylthiazol-4-yl}ethoxy]benzothien-2-yl)-1-(diethoxyphosphinyl)eth-1-yl]-1,3,2-dioxaphospholane-2-oxide;
- 2[2-(5-[3-{5-methyl-2-pyrid-4-yloxazol-4-yl}-1-oxoprop-1-yl]benzothien-2-yl)-1-(diethoxyphosphinyl)eth-1-yl]-1,3,2-dioxaphospholane-2-oxide;
- 10 *N,N,N',N'*-Tetramethyl-1 (5-[*N*-(2-{5-methyl-2-pyrid-4-ylthiazol-4-yl}ethyl)-*N*-methylamino]benzothien-2-yl)-1-hydroxymethylphosphondiamide;
- N,N'*-Diethyl 1-(5-[2-{4-(4-trifluoromethylphenyl)phenoxy}ethoxy]benzothien-2-yl)-1-hydroxymethylphosphondiamide;
- 15 2-[1-hydroxy-1-(5-[*N*-(2-{4-(4-trifluoromethylphenyl)phenoxy}ethyl)-*N*-methylamino]benzothien-2-yl)methyl]-[4*S*,5*S*]-dimethyl-1,3,2-diazaphospholidine-2-oxide;
- 2-[1-hydroxy-1-(5-[3-{4-(4-trifluoromethylphenyl)phenoxy}-1-oxoprop-1-yl]benzothien-2-yl)methyl]-1,3,5,5-tetramethyl-1,3,2-diazaphosphinane-2-oxide;
- 20 2-[1-hydroxy-1-(5-[2-{1-[4-(2-trifluoromethylphenyl)phenylmethyl]-3-hexylureido}ethyl]benzothien-2-yl)methyl]-[4*S*]-ethyl-1,3,2-oxazaphospholidine-2-oxide;
- 2-[1-hydroxy-1-(5-[2-{1-butyl-3-(5-methoxypyrid-2-yl)ureido}ethyl]benzothien-2-yl)methyl]-[4*R*]-methyl-1,3,2-oxazaphosphinane-2-oxide;

- N,N,N',N'*-Tetramethyl-1 (5-[3-{4-acetyl-3-hydroxy-2-propylphenoxy}propoxy]benzothien-2-yl)-1-hydroxymethylphosphondiamide;
- N,N'*-Diethyl 1-(5-[2-{4*H*-3-oxobenzo[1,4]oxazin-2-yl}ethoxy]benzothien-2-yl)-1-hydroxymethylphosphondiamide;
- 5 2-[1-hydroxy-1-(5-[3,*N*-phthalimidopropoxy]benzothien-2-yl)methyl]-[4*S*,5*S*]-dimethyl-1,3,2-diazaphospholidine-2-oxide;
- 2-[1-hydroxy-1-(5-[4,*N*-phthalimidobutoxy]benzothien-2-yl)methyl]-1,3,5,5-tetramethyl-1,3,2-diazaphosphinane-2-oxide;
- 2-[1-hydroxy-1-(4-[2-{*N*-methyl-*N*-pyrid-2-ylamino}ethoxy]thiazol-2-yl)methyl]-[4*S*]-ethyl-1,3,2-oxazaphospholidine-2-oxide;
- 10 2-[1-hydroxy-1-(4-[*N*-(2-{*N*-methyl-*N*-pyrid-2-ylamino}ethyl)-*N*-methylamino]thiazol-2-yl)methyl]-[4*R*]methyl-1,3,2-oxazaphosphinane-2-oxide;
- N,N,N',N'*-Tetramethyl 1-(4-[3-{*N*-methyl-*N*-pyrid-2-ylamino}-1-oxoprop-1-yl]thiazol-2-yl)-1-(bis[*N,N*-dimethylamino]phosphoryloxy)methylphosphondiamide;
- 15 *N,N'*-Diethyl 1-(4-[2-{5-methyl-2-phenyloxazol-4-yl}ethoxy]thiazol-2-yl)-1-(bis[*N*-ethylamino]phosphoryloxy)methylphosphondiamide;
- 2-[1-{([4*S*,5*S*]-dimethyl-2-oxido-1,3,2-diazaphospholidin-2-yl)oxy}-1-(4-[*N*-(2-{5-methyl-2-phenyloxazol-4-yl}ethyl)-*N*-methylamino]thiazol-2-yl)methyl]-[4*S*,5*S*]-dimethyl-1,3,2-diazaphospholidine-2-oxide;
- 20 2-[1-{(1,3,5,5-tetramethyl-2-oxido-1,3,2-diazaphosphinan-2-yl)oxy}-1-(4-[2-{5-methyl-2-phenylthiazol-4-yl}ethoxy]thiazol-2-yl)methyl]-1,3,5,5-tetramethyl-1,3,2-diazaphosphinane-2-oxide;
- 2-[1-{(4*S*)-ethyl-2-oxido-1,3,2-oxazaphospholidin-2-yl)oxy}-1-(4-[3-{5-methyl-2-phenylthiazol-4-yl}-1-oxoprop-1-yl]thiazol-2-yl)methyl]-[4*S*]-ethyl-1,3,2-
- 25 oxazaphospholidine-2-oxide;

- 2-[1-{([4R]methyl-1,3,2-oxazaphosphinan-2-yl)oxy}-1-(4-[2-{5-methyl-2-pyrid-4-yloxazol-4-yl}ethoxy]thiazol-2-yl)methyl]-[4R]methyl-1,3,2-oxazaphosphinane-2-oxide;
- N,N,N',N'*-Tetramethyl 1-(4-[2-{5-methyl-2-pyrid-4-ylthiazol-4-yl}ethoxy]thiazol-2-yl)-  
 5 1-(bis[*N,N*-dimethylamino]phosphoryloxy)methylphosphondiamide;  
*N,N'*-Diethyl 1-(4-[3-{5-methyl-2-pyrid-4-yloxazol-4-yl}-1-oxoprop-1-yl]thiazol-2-yl)-1-(bis[*N*-ethylamino]phosphoryloxy)methylphosphondiamide;
- 2-[1-{([4S,5S]-dimethyl-2-oxido-1,3,2-diazaphospholidin-2-yl)oxy}-1-(4-[*N*-(2-{5-methyl-2-pyrid-4-ylthiazol-4-yl}ethyl)-*N*-methylamino]thiazol-2-yl)methyl]-[4S,5S]-  
 10 dimethyl-1,3,2-diazaphospholidine-2-oxide;
- 2-[1-{(1,3,5,5-tetramethyl-2-oxido-1,3,2-diazaphosphinan-2-yl)oxy}-1-(4-[2-{4-(4-trifluoromethylphenyl)phenoxy}ethoxy]thiazol-2-yl)methyl]-1,3,5,5-tetramethyl-1,3,2-diazaphosphinane-2-oxide;
- 2-[1-{(4S)-ethyl-2-oxido-1,3,2-oxazaphospholidin-2-yl)oxy}-1-(4-[*N*-(2-{4-(4-trifluoromethylphenyl)phenoxy}ethyl)-*N*-methylamino]thiazol-2-yl)methyl]-[4S]-  
 15 ethyl-1,3,2-oxazaphospholidine-2-oxide;
- 2-[1-{([4R]methyl-1,3,2-oxazaphosphinan-2-yl)oxy}-1-(4-[3-{4-(4-trifluoromethylphenyl)phenoxy}-1-oxoprop-1-yl]thiazol-2-yl)methyl]-[4R]methyl-1,3,2-oxazaphosphinane-2-oxide;
- 20 1-(4-[2-{1-[4-(2-trifluoromethylphenyl)phenylmethyl]-3-hexylureido}ethyl]thiazol-2-yl)-1,1-bis(bis[*N,N*-dimethylamino]phosphoryl)methane;
- 1-(4-[2-{1-butyl-3-(5-methoxypyrid-2-yl)ureido}ethyl]thiazol-2-yl)-1,1-bis(bis[*N*-ethylamino]phosphoryl)methane;
- 1-(4-[3-{4-acetyl-3-hydroxy-2-propylphenoxy}propoxy]thiazol-2-yl)-1,1-bis([4S,5S]-  
 25 dimethyl-2-oxido-1,3,2-diazaphospholidin-2-yl)methane;

- 1-(4-[2-{4*H*-3-oxobenzo[1,4]oxazin-2-yl}ethoxy]thiazol-2-yl)-1,1-bis(1,3,5,5-tetramethyl-2-oxido-1,3,2-diazaphosphinan-2-yl)methane;
- 1-(4-[3,*N*-phthalimidopropoxy]thiazol-2-yl)-1,1-bis ([4*S*]-ethyl-2-oxido-1,3,2-oxazaphospholidin-2-yl)methane;
- 5 1-(4-[4,*N*-phthalimidobutoxy]thiazol-2-yl)-1,1-bis ([4*R*]-methyl-2-oxido-1,3,2-oxazaphosphinan-2-yl)methane;
- 1-(6-[2-{*N*-methyl-*N*-pyrid-2-ylamino}ethoxy]-3-methoxyquinolin-2-yl)-1,1-bis(bis[*N,N*-dimethylamino]phosphoryl)methane;
- 1-(6-[*N*-(2-{*N*-methyl-*N*-pyrid-2-ylamino}ethyl)-*N*-methylamino]-3-methoxyquinolin-2-yl)-1,1-bis(bis[*N*-ethylamino]phosphoryl)methane;
- 10 1-(6-[3-{*N*-methyl-*N*-pyrid-2-ylamino}-1-oxoprop-1-yl]-3-methoxyquinolin-2-yl)-1,1-bis([4*S*,5*S*]-dimethyl-2-oxido-1,3,2-diazaphospholidin-2-yl)methane;
- 1-(6-[2-{5-methyl-2-phenyloxazol-4-yl}ethoxy]-3-methoxyquinolin-2-yl)-1,1-bis(1,3,5,5-tetramethyl-2-oxido-1,3,2-diazaphosphinan-2-yl)methane;
- 15 1-(6-[*N*-(2-{5-methyl-2-phenyloxazol-4-yl}ethyl)-*N*-methylamino]-3-methoxyquinolin-2-yl)-1,1-bis ([4*S*]-ethyl-2-oxido-1,3,2-oxazaphospholidin-2-yl)methane;
- 1-(6-[2-{5-methyl-2-phenylthiazol-4-yl}ethoxy]-3-methoxyquinolin-2-yl)-1,1-bis ([4*R*]-methyl-2-oxido-1,3,2-oxazaphosphinan-2-yl)methane;
- 1-(6-[3-{5-methyl-2-phenylthiazol-4-yl}-1-oxoprop-1-yl]-3-methoxyquinolin-2-yl)-1,2-bis(bis[*N,N*-dimethylamino]phosphoryl)ethane;
- 20 1-(6-[2-{5-methyl-2-pyrid-4-yloxazol-4-yl}ethoxy]-3-methoxyquinolin-2-yl)-1,2-bis(bis[*N*-ethylamino]phosphoryl)ethane;
- 1-(6-[2-{5-methyl-2-pyrid-4-ylthiazol-4-yl}ethoxy]-3-methoxyquinolin-2-yl)-1,2-bis([4*S*,5*S*]-dimethyl-2-oxido-1,3,2-diazaphospholidin-2-yl)ethane;

- 1-(6-[3-{5-methyl-2-pyrid-4-yloxazol-4-yl}-1-oxoprop-1-yl]-3-methoxyquinolin-2-yl)-  
1,2-bis(1,3,5,5-tetramethyl-2-oxido-1,3,2-diazaphosphinan-2-yl)ethane;
- 1-(6-[*N*-(2-{5-methyl-2-pyrid-4-ylthiazol-4-yl}ethyl)-*N*-methylamino]-3-  
methoxyquinolin-2-yl)-1,2-bis ([4*S*]-ethyl-2-oxido-1,3,2-oxazaphospholidin-2-  
5 yl)ethane;
- 1-(6-[2-{4-(4-trifluoromethylphenyl)phenoxy}ethoxy]-3-methoxyquinolin-2-yl)-1,2-bis  
([4*R*]methyl-2-oxido-1,3,2-oxazaphosphinan-2-yl)ethane;
- 1-(6-[*N*-(2-{4-(4-trifluoromethylphenyl)phenoxy}ethyl)-*N*-methylamino]-3-  
methoxyquinolin-2-yl)-1,2-bis(bis[*N,N*-dimethylamino]phosphoryl)ethane;
- 10 1-(6-[3-{4-(4-trifluoromethylphenyl)phenoxy}-1-oxoprop-1-yl]-3-methoxyquinolin-2-yl)-  
1,2-bis(bis[*N*-ethylamino]phosphoryl)ethane;
- 1-(6-[2-{1-[4-(2-trifluoromethylphenyl)phenylmethyl]-3-hexylureido}ethyl]-3-  
methoxyquinolin-2-yl)-1,2-bis([4*S*,5*S*]-dimethyl-2-oxido-1,3,2-diazaphospholidin-2-  
yl)ethane;
- 15 1-(6-[2-{1-butyl-3-(5-methoxypyrid-2-yl)ureido}ethyl]-3-methoxyquinolin-2-yl)-1,2-  
bis(1,3,5,5-tetramethyl-2-oxido-1,3,2-diazaphosphinan-2-yl)ethane;
- 1-(6-[3-{4-acetyl-3-hydroxy-2-propylphenoxy}propoxy]-3-methoxyquinolin-2-yl)-1,2-bis  
([4*S*]-ethyl-2-oxido-1,3,2-oxazaphospholidin-2-yl)ethane;
- 1-(6-[3,*N*-phthalimidopropoxy]-3-methoxyquinolin-2-yl)-1,2-bis ([4*R*]methyl-2-oxido-  
20 1,3,2-oxazaphosphinan-2-yl)ethane;
- 2-(6-[4,*N*-phthalimidobutoxy]-3-methoxyquinolin-2-yl)-1,1-bis(bis[*N,N*-  
dimethylamino]phosphoryl)ethane;
- 2-(5-[2-{*N*-methyl-*N*-pyrid-2-ylamino}ethoxy]thien-2-yl)-1,1-bis(bis[*N*-  
ethylamino]phosphoryl)ethane;

- 2-(5-[*N*-(2-{*N*-methyl-*N*-pyrid-2-ylamino}ethyl)-*N*-methylamino]thien-2-yl)-1,1-bis([4*S*,5*S*]-dimethyl-2-oxido-1,3,2-diazaphospholidin-2-yl)ethane;
- 2-(5-[3-{*N*-methyl-*N*-pyrid-2-ylamino}-1-oxoprop-1-yl]thien-2-yl)-1,1-bis(1,3,5,5-tetramethyl-2-oxido-1,3,2-diazaphosphinan-2-yl)ethane;
- 5 2-(5-[2-{5-methyl-2-phenyloxazol-4-yl}ethoxy]thien-2-yl)-1,1-bis([4*S*]-ethyl-2-oxido-1,3,2-oxazaphospholidin-2-yl)ethane;
- 2-(5-[*N*-(2-{5-methyl-2-phenyloxazol-4-yl}ethyl)-*N*-methylamino]thien-2-yl)-1,1-bis([4*R*]methyl-2-oxido-1,3,2-oxazaphosphinan-2-yl)ethane;
- 2-(5-[2-{5-methyl-2-phenylthiazol-4-yl}ethoxy]thien-2-yl)-1,1-bis(bis[*N,N*-
- 10 dimethylamino]phosphoryl)ethane;
- 2-(5-[3-{5-methyl-2-phenylthiazol-4-yl}-1-oxoprop-1-yl]thien-2-yl)-1,1-bis(bis[*N*-ethylamino]phosphoryl)ethane;
- 2-(5-[2-{5-methyl-2-pyrid-4-ylloxazol-4-yl}ethoxy]thien-2-yl)-1,1-bis([4*S*,5*S*]-dimethyl-2-oxido-1,3,2-diazaphospholidin-2-yl)ethane;
- 15 2-(5-[2-{5-methyl-2-pyrid-4-ylthiazol-4-yl}ethoxy]thien-2-yl)-1,1-bis(1,3,5,5-tetramethyl-2-oxido-1,3,2-diazaphosphinan-2-yl)ethane;
- 2-(5-[3-{5-methyl-2-pyrid-4-ylloxazol-4-yl}-1-oxoprop-1-yl]thien-2-yl)-1,1-bis([4*S*]-ethyl-2-oxido-1,3,2-oxazaphospholidin-2-yl)ethane;
- 2-(5-[*N*-(2-{5-methyl-2-pyrid-4-ylthiazol-4-yl}ethyl)-*N*-methylamino]thien-2-yl)-1,1-bis
- 20 ([4*R*]methyl-2-oxido-1,3,2-oxazaphosphinan-2-yl)ethane;
- 1-[*N*-(5-[2-{4-(4-trifluoromethylphenyl)phenoxy}ethoxy]thien-2-yl)amino]-1,1-bis(bis[*N,N*-dimethylamino]phosphoryl)methane;
- 1-[*N*-(5-[*N*-(2-{4-(4-trifluoromethylphenyl)phenoxy}ethyl)-*N*-methylamino]thien-2-yl)amino]-1,1-bis(bis[*N*-ethylamino]phosphoryl)methane;



- 1-[*N*-(5-[3-{4-(4-trifluoromethylphenyl)phenoxy}-1-oxoprop-1-yl]thien-2-yl)amino]-1,1-bis([4*S*,5*S*]-dimethyl-2-oxido-1,3,2-diazaphospholidin-2-yl)methane;
- 1-[*N*-(5-[2-{1-[4-(2-trifluoromethylphenyl)phenylmethyl]-3-hexylureido}ethyl]thien-2-yl)amino]-1,1-bis(1,3,5,5-tetramethyl-2-oxido-1,3,2-diazaphosphinan-2-yl)methane;
- 5 1-[*N*-(5-[2-{1-butyl-3-(5-methoxypyrid-2-yl)ureido}ethyl]thien-2-yl)amino]-1,1-bis([4*S*]-ethyl-2-oxido-1,3,2-oxazaphospholidin-2-yl)methane;
- 1-[*N*-(5-[3-{4-acetyl-3-hydroxy-2-propylphenoxy}propoxy]thien-2-yl)amino]-1,1-bis([4*R*]-methyl-2-oxido-1,3,2-oxazaphosphinan-2-yl)methane;
- 1-[*N*-(5-[2-{4*H*-3-oxobenzo[1,4]oxazin-2-yl}ethoxy]thien-2-yl)amino]-1,1-bis(bis[*N,N*-dimethylamino]phosphoryl)methane;
- 10 1-[*N*-(5-[3,*N*-phthalimidopropoxy]thien-2-yl)amino]-1,1-bis(bis[*N*-ethylamino]phosphoryl)methane;
- 1-[*N*-(5-[4,*N*-phthalimidobutoxy]thien-2-yl)amino]-1,1-bis([4*S*,5*S*]-dimethyl-2-oxido-1,3,2-diazaphospholidin-2-yl)methane;
- 15 1-[*N*-(4-[2-{*N*-methyl-*N*-pyrid-2-ylamino}ethoxy]-3-fluorophenyl)amino]-1,1-bis(1,3,5,5-tetramethyl-2-oxido-1,3,2-diazaphosphinan-2-yl)methane;
- 1-[*N*-(4-[*N*-(2-{*N*-methyl-*N*-pyrid-2-ylamino}ethyl)-*N*-methylaminocarbonyl]-3-fluorophenyl)amino]-1,1-bis([4*S*]-ethyl-2-oxido-1,3,2-oxazaphospholidin-2-yl)methane;
- 20 1-[*N*-(4-[3-{*N*-methyl-*N*-pyrid-2-ylamino}-1-oxoprop-1-yl]-3-fluorophenyl)amino]-1,1-bis([4*R*]-methyl-2-oxido-1,3,2-oxazaphosphinan-2-yl)methane;
- 2-[1-(Bis[*N*-ethylamino]phosphoryloxy)-1-(4-[2-{5-methyl-2-phenyloxazol-4-yl}ethoxy]-3-fluorophenyl)methyl]-[4*S*,5*S*]-dimethyl-1,3,2-diazaphospholidine-2-oxide;

- 2-[1-(Bis[*N*-ethylamino]phosphoryl)-1-(4-[*N*-(2-{5-methyl-2-phenyloxazol-4-yl} ethyl)-*N*-methylaminocarbonyl]-3-fluorophenyl)methoxy]-[4*S*,5*S*]-dimethyl-1,3,2-diazaphospholidine-2-oxide;
- 2-[1-(Bis[*N*-ethylamino]phosphoryl)-1-(4-[2-{5-methyl-2-phenylthiazol-4-yl} ethoxy]-3-fluorophenyl)methyl]-1,3,5,5-tetramethyl-1,3,2-diazaphosphinane-2-oxide;
- 2-[1-(Bis[*N*-ethylamino]phosphoryl)-2-(4-[3-{5-methyl-2-phenylthiazol-4-yl}-1-oxoprop-1-yl]-3-fluorophenyl)ethen-1-yl]-[4*S*]-ethyl-1,3,2-oxazaphospholidine-2-oxide;
- 2-[1-(Bis[*N*-ethylamino]phosphoryl)-2-(4-[2-{5-methyl-2-pyrid-4-yloxazol-4-yl} ethoxy]-3-fluorophenyl)eth-1-yl]-[4*R*]-methyl-1,3,2-oxazaphosphinane-2-oxide;
- 2-[2-(Bis[*N*-ethylamino]phosphoryl)-2-(4-[2-{5-methyl-2-pyrid-4-ylthiazol-4-yl} ethoxy]-3-fluorophenyl)eth-1-yl]-1,3,5,5-tetramethyl-1,3,2-diazaphosphinane-2-oxide;
- 2-[2-(Bis[*N*-ethylamino]phosphoryl)-1-(4-[3-{5-methyl-2-pyrid-4-yloxazol-4-yl}-1-oxoprop-1-yl]-3-fluorophenyl)eth-1-yl]-[4*S*]-ethyl-1,3,2-oxazaphospholidine-2-oxide;
- 2-[1-(Bis[*N*-ethylamino]phosphoryloxy)-1-(4-[*N*-(2-{5-methyl-2-pyrid-4-ylthiazol-4-yl} ethyl)-*N*-methylaminocarbonyl]-3-fluorophenyl)methyl]-[4*S*,5*S*]-dimethyl-1,3,2-diazaphospholidine-2-oxide;
- 2-[1-(Bis[*N*-ethylamino]phosphoryl)-1-(4-[2-{4-(4-trifluoromethylphenyl)phenoxy} ethoxy]-3-fluorophenyl)methoxy]-[4*S*,5*S*]-dimethyl-1,3,2-diazaphospholidine-2-oxide;
- 2-[1-(Bis[*N*-ethylamino]phosphoryl)-1-(4-[*N*-(2-{4-(4-trifluoromethylphenyl)phenoxy} ethyl)-*N*-methylaminocarbonyl]-3-fluorophenyl)methyl]-1,3,5,5-tetramethyl-1,3,2-diazaphosphinane-2-oxide;
- 2-[1-(Bis[*N*-ethylamino]phosphoryl)-2-(4-[3-{4-(4-trifluoromethylphenyl)phenoxy}-1-oxoprop-1-yl]-3-fluorophenyl)ethen-1-yl]-[4*S*]-ethyl-1,3,2-oxazaphospholidine-2-oxide;

- 2-[1-(Bis[*N*-ethylamino]phosphoryl)-2-(4-[2-{1-[4-(2-trifluoromethylphenyl)phenylmethyl]-3-hexylureido}ethyl]-3-fluorophenyl)eth-1-yl]-[4R]methyl-1,3,2-oxazaphosphinane-2-oxide;
- 2-[2-(Bis[*N*-ethylamino]phosphoryl)-2-(4-[2-{1-butyl-3-(5-methoxypyrid-2-yl)ureido}ethyl]-3-fluorophenyl)eth-1-yl]-1,3,5,5-tetramethyl-1,3,2-diazaphosphinane-2-oxide;
- 2-[2-(Bis[*N*-ethylamino]phosphoryl)-1-(4-[3-{4-acetyl-3-hydroxy-2-propylphenoxy}propoxy]-3-fluorophenyl)eth-1-yl]-[4S]-ethyl-1,3,2-oxazaphospholidine-2-oxide;
- 2-[1-(Diethoxyphosphoryloxy)-1-(4-[2-{4*H*-3-oxobenzo[1,4]oxazin-2-yl}ethoxy]-3-fluorophenyl)methyl]-[4S,5S]-dimethyl-1,3,2-diazaphospholidine-2-oxide;
- 2-[1-(Diethoxyphosphoryl)-1-(4-[3,*N*-phthalimidopropoxy]-3-fluorophenyl)methoxy]-[4S,5S]-dimethyl-1,3,2-diazaphospholidine-2-oxide;
- 2-[1-(Diethoxyphosphoryl)-1-(4-[4,*N*-phthalimidobutoxy]-3-fluorophenyl)methyl]-1,3,5,5-tetramethyl-1,3,2-diazaphosphinane-2-oxide;
- 2-[1-(Diethoxyphosphoryl)-2-(3-[3-{*N*-methyl-*N*-pyrid-2-ylamino}propoxy]-4-fluorophenyl)ethen-1-yl]-[4S]-ethyl-1,3,2-oxazaphospholidine-2-oxide;
- 2-[1-(Diethoxyphosphoryl)-2-(3-[*N*-(3-{*N*-methyl-*N*-pyrid-2-ylamino}propyl)-*N*-methylamino]-4-fluorophenyl)eth-1-yl]-[4R]methyl-1,3,2-oxazaphosphinane-2-oxide;
- 2-[2-(Diethoxyphosphoryl)-2-(3-[3-{*N*-methyl-*N*-pyrid-2-ylamino}-1-oxoprop-1-ylamino]-4-fluorophenyl)eth-1-yl]-1,3,5,5-tetramethyl-1,3,2-diazaphosphinane-2-oxide;
- 2-[2-(Diethoxyphosphoryl)-1-(3-[3-{5-methyl-2-phenyloxazol-4-yl}propoxy]-4-fluorophenyl)eth-1-yl]-[4S]-ethyl-1,3,2-oxazaphospholidine-2-oxide;

- 2-[1-(Diethoxyphosphoryloxy)-1-(3-[*N*-(2-{5-methyl-2-phenyloxazol-4-yl}ethyl)-*N*-methylaminocarbonyl]-4-methoxyphenyl)methyl]-[4*S*,5*S*]-dimethyl-1,3,2-diazaphospholidine-2-oxide;
- 2-[1-(Diethoxyphosphoryl)-1-(3-[3-{5-methyl-2-phenylthiazol-4-yl}propoxy]-4-fluorophenyl)methoxy]-[4*S*,5*S*]-dimethyl-1,3,2-diazaphospholidine-2-oxide;
- 2-[1-(Diethoxyphosphoryl)-1-(3-[3-{5-methyl-2-phenylthiazol-4-yl}-1-oxoprop-1-yl]-4-fluorophenyl)methyl]-1,3,5,5-tetramethyl-1,3,2-diazaphosphinane-2-oxide;
- 2-[1-(Diethoxyphosphoryl)-2-(3-[4-{5-methyl-2-pyrid-4-yloxazol-4-yl}butoxy]-4-fluorophenyl)ethen-1-yl]-[4*S*]-ethyl-1,3,2-oxazaphospholidine-2-oxide;
- 2-[1-(Diethoxyphosphoryl)-2-(3-[3-{5-methyl-2-pyrid-4-ylthiazol-4-yl}propoxy]-4-fluorophenyl)eth-1-yl]-[4*R*]-methyl-1,3,2-oxazaphosphinane-2-oxide;
- 2-[2-(Diethoxyphosphoryl)-2-(3-[3-{5-methyl-2-pyrid-4-yloxazol-4-yl}-1-oxoprop-1-ylthio]-4-fluorophenyl)eth-1-yl]-1,3,5,5-tetramethyl-1,3,2-diazaphosphinane-2-oxide;
- and
- 2-[2-(Diethoxyphosphoryl)-1-(3-[*N*-(3-{5-methyl-2-pyrid-4-ylthiazol-4-yl}propyl)-*N*-methylamino]-4-fluorophenyl)eth-1-yl]-[4*S*]-ethyl-1,3,2-oxazaphospholidine-2-oxide.

In an even more preferred embodiment of this aspect, the compound of Formula

(I) is selected from:

- Diethyl 1-(diethoxyphosphinyloxy)-1-(4-[2-{*N*-methyl-*N*-pyrid-2-ylamino}ethoxy]-3-fluorophenyl)methylphosphonate;
- Diethyl 1-(diethoxyphosphinyloxy)-1-(4-[3,*N*-phthalimidopropoxy]-3-fluorophenyl)methylphosphonate;
- Diethyl 1-(diethoxyphosphinyloxy)-1-(4-[2-{5-methyl-2-phenyloxazol-4-yl}ethoxy]-3-fluorophenyl)methylphosphonate;

- Diethyl 1-(diethoxyphosphinyloxy)-1-(3-[3-{*N*-methyl-*N*-pyrid-2-ylamino}propoxy]-4-fluorophenyl)methylphosphonate;
- Diethyl 1-(diethoxyphosphinyloxy)-1-(3-[4-{*N*-methyl-*N*-pyrid-2-ylamino}butoxy]-4-fluorophenyl)methylphosphonate;
- 5 Diethyl 1-(diethoxyphosphinyloxy)-1-(3-[4,*N*-phthalimidobutoxy]-4-fluorophenyl)methylphosphonate;
- Diethyl 1-(diethoxyphosphinyloxy)-1-(3-[5,*N*-phthalimidopentoxy]-4-fluorophenyl)methylphosphonate;
- Diethyl 1-(diethoxyphosphinyloxy)-1-(3-[4-{5-methyl-2-pyrid-4-yloxazol-4-yl}butoxy]-
- 10 4-fluorophenyl)methylphosphonate;
- Diethyl 1-(diethoxyphosphinyloxy)-1-(3-[5-{5-methyl-2-pyrid-4-yloxazol-4-yl}pentoxy]-4-fluorophenyl)methylphosphonate;
- 1-(4-[2-{*N*-methyl-*N*-pyrid-2-ylamino}ethoxy]-3-fluorophenyl)-1,1-bis([4*R*,5*S*]-dimethyl-2-oxido-1,3,2-dioxaphospholan-2-yl)methane;
- 15 1-(4-[3,*N*-phthalimidopropoxy]-3-fluorophenyl)-1,1-bis([4*R*,5*S*]-dimethyl-2-oxido-1,3,2-dioxaphospholan-2-yl)methane;
- 1-(4-[2-{5-methyl-2-phenyloxazol-4-yl}ethoxy]-3-fluorophenyl)-1,1-bis([4*R*,5*S*]-dimethyl-2-oxido-1,3,2-dioxaphospholan-2-yl)methane;
- 1-(3-[3-{*N*-methyl-*N*-pyrid-2-ylamino}propoxy]-4-fluorophenyl)-1,1-bis([4*R*,5*S*]-
- 20 dimethyl-2-oxido-1,3,2-dioxaphospholan-2-yl)methane;
- 1-(3-[4-{*N*-methyl-*N*-pyrid-2-ylamino}butoxy]-4-fluorophenyl)-1,1-bis([4*R*,5*S*]-dimethyl-2-oxido-1,3,2-dioxaphospholan-2-yl)methane;
- 1-(3-[4,*N*-phthalimidobutoxy]-4-fluorophenyl)-1,1-bis([4*R*,5*S*]-dimethyl-2-oxido-1,3,2-dioxaphospholan-2-yl)methane;

- 1-(3-[5,*N*-phthalimidopentoxy]-4-fluorophenyl)-1,1-bis([4*R*,5*S*]-dimethyl-2-oxido-1,3,2-dioxaphospholan-2-yl)methane;
- 1-(3-[4-{5-methyl-2-pyrid-4-yloxazol-4-yl}butoxy]-4-fluorophenyl)-1,1-bis([4*R*,5*S*]-dimethyl-2-oxido-1,3,2-dioxaphospholan-2-yl)methane;
- 5 1-(3-[5-{5-methyl-2-pyrid-4-yloxazol-4-yl}pentoxy]-4-fluorophenyl)-1,1-bis([4*R*,5*S*]-dimethyl-2-oxido-1,3,2-dioxaphospholan-2-yl)methane;
- N,N,N',N'*-Tetramethyl 1-(4-[2-{*N*-methyl-*N*-pyrid-2-ylamino}ethoxy]-3-fluorophenyl)-1-hydroxymethylphosphondiamide;
- N,N,N',N'*-Tetramethyl 1-(4-[3,*N*-phthalimidopropoxy]-3-fluorophenyl)-1-
- 10 hydroxymethylphosphondiamide;
- N,N,N',N'*-Tetramethyl 1-(4-[2-{5-methyl-2-phenyloxazol-4-yl}ethoxy]-3-fluorophenyl)-1-hydroxymethylphosphondiamide;
- 2-[1-hydroxy-1-(4-[2-{*N*-methyl-*N*-pyrid-2-ylamino}ethoxy]-3-fluorophenyl)methyl]-[4*S*]-1-methylethyl)-1,3,2-oxazaphospholidine-2-oxide;
- 15 2-[1-hydroxy-1-(4-[3,*N*-phthalimidopropoxy]-3-fluorophenyl)methyl]-[4*S*]-1-methylethyl)-1,3,2-oxazaphospholidine-2-oxide;
- 2-[1-hydroxy-1-(4-[2-{5-methyl-2-phenyloxazol-4-yl}ethoxy]-3-fluorophenyl)methyl]-[4*S*]-1-methylethyl)-1,3,2-oxazaphospholidine-2-oxide;
- 1-[*N*-(4-[2-{*N*-methyl-*N*-pyrid-2-ylamino}ethoxy]-3-fluorophenyl)amino]-1,1-bis(bis[*N*-
- 20 ethylamino]phosphoryl)methane;
- 1-[*N*-(4-[3,*N*-phthalimidopropoxy]-3-fluorophenyl)amino]-1,1-bis(bis[*N*-ethylamino]phosphoryl)methane; and
- 1-[*N*-(4-[2-{5-methyl-2-phenyloxazol-4-yl}ethoxy]-3-fluorophenyl)amino]-1,1-bis(bis[*N*-ethylamino]phosphoryl)methane.

In another aspect, the invention provides methods for regulating levels of HDL and/or LDL cholesterol levels in blood, comprising administering to a subject a compound of the invention, or pharmaceutical formulation comprising a compound of the invention, or a pharmaceutically acceptable salt thereof, in an amount effective to regulate  
5 HDL and/or LDL cholesterol levels. This method of regulating HDL and/or LDL levels in blood can help prevent, treat, or delay the onset or progression of disease states associated with abnormal blood levels of HDL and/or LDL.

In another aspect, the invention provides methods for treating disease states related to HDL and/or LDL cholesterol levels in blood, comprising administering to a  
10 subject in need of such treatment, a therapeutically effective amount of a compound of the invention, or pharmaceutical formulation comprising a compound of the invention, or a pharmaceutically acceptable salt thereof.

In another embodiment of this aspect, the method can optionally comprise in combination with the compound of Formula (I), pharmaceutical formulation comprising a  
15 compound of Formula (I), or pharmaceutically acceptable salts thereof, an effective amount of a compound known to regulate HDL and/or LDL levels in blood. Such known compounds include the non-limiting classes of compounds such as statins, for example, lovastatin, simvastatin, pravastatin, atorvastatin, cerivastatin, and niacin; fibrates, for example, clofibrate, bezafibrate, and gemfibrozil; bile acid sequestrants, for example,  
20 cholestyramine; and cholesterol uptake inhibitors, for example, phytosteroids, and ezetimibe.

In another aspect, the invention provides methods for lowering triglyceride levels in blood, comprising administering to a subject in need of such treatment, a therapeutically effective amount of a compound of the invention, or pharmaceutical

formulation comprising a compound of the invention, or a pharmaceutically acceptable salt thereof.

In another embodiment of this aspect, the method can optionally comprise in combination with the compound of Formula (I), pharmaceutical formulation comprising a compound of Formula (I), or pharmaceutically acceptable salts thereof, an effective  
5 amount of a compound known to lower triglyceride levels in blood. Such known compounds include the non-limiting example of fibrates, for example, clofibrate, bezafibrate, and gemfibrozil.

In another aspect, the invention provides methods for lowering glucose levels in  
10 blood, comprising administering to a subject in need of such treatment, a therapeutically effective amount of a compound of the invention, or pharmaceutical formulation comprising a compound of the invention, or a pharmaceutically acceptable salt thereof.

In another embodiment of this aspect, the method can optionally comprise in combination with the compound of Formula (I), pharmaceutical formulation comprising a  
15 compound of Formula (I), or pharmaceutically acceptable salts thereof, an effective amount of a compound known to lower glucose levels in blood. Such known compounds include the non-limiting classes glitazones, such as rosiglitazone and pioglitazone; sulfonylureas; insulin; and metformin.

In another aspect, the methods of treatment can treat an existing metabolic  
20 disease, such as hypercholesteremia, hypertriglyceridemia, low HDL-C atherosclerosis, hyperglycemia, syndrome X, hyperinsulinemia, and diabetes.

In another aspect, the methods of treatment can prevent a metabolic disease, such as hypercholesteremia, hypertriglyceridemia, low HDL-C atherosclerosis, hyperglycemia, syndrome X, hyperinsulinemia, and diabetes, from developing or progressing.



In one embodiment of the methods of the invention, the subject is a mammal. In a more preferred embodiment, the mammal is a human.

The methods of the invention employ therapeutically effective amounts: for oral, parenteral, sublingual, intranasal, intrathecal, depo, implants, topical, and rectal  
5 administration from about 0.1 mg/day to about 5,000 mg/day. The therapeutically effective amounts will vary according to various parameters including, for example, the particular therapeutic use and physical characteristics of the subject/patient, and are well within the knowledge of those skilled in the art.

In a preferred aspect, the therapeutically effective amounts for oral, parenteral,  
10 and depo administration is from about 50 mg/day to about 500 mg/day.

The present invention also includes the use of a compound of Formula (I), or a pharmaceutically acceptable salt thereof for the manufacture of a medicament for use in treating a subject who has, or in preventing a subject from developing, a metabolic disease, condition, or disorder, such as, for example, hypercholesteremia,  
15 hypertriglyceridemia, low HDL-C atherosclerosis, hyperglycemia, syndrome X, hyperinsulinemia, and diabetes and who is in need of such treatment.

In one aspect, this use of a compound of formula (I) can be employed where the disease is hypercholesteremia.

In another aspect, this use of a compound of formula (I) can be employed where  
20 the disease is hypertriglyceridemia.

In another aspect, this use of a compound of formula (I) can be employed where the disease is low HDL-C atherosclerosis.

In another aspect, this use of a compound of formula (I) can be employed where the disease is hyperglycemia.

In another aspect, this use of a compound of formula (I) can be employed where the disease is syndrome X.

In another aspect, this use of a compound of formula (I) can be employed where the disease is hyperinsulinemia.

5        In another aspect, this use of a compound of formula (I) can be employed where the disease is diabetes.

The present invention also includes a container kit including a plurality of containers, each container including one or more unit dose of a compound of formula (I), or a pharmaceutically acceptable salt thereof.

10        In an embodiment, this container kit includes each container adapted for oral delivery and includes a tablet, gel, or capsule.

In an embodiment, this container kit includes each container adapted for parenteral delivery and includes a depot product, syringe, ampoule, or vial.

15        In an embodiment, this container kit includes each container adapted for topical delivery and includes a patch, medipad, ointment, or cream.

The present invention also includes an agent kit including a compound of formula (I), or a pharmaceutically acceptable salt thereof; and one or more therapeutic agents selected from the group consisting of statins, fibrates, bile acid sequestrants, cholesterol uptake inhibitors, glitazones, sulfonylureas, insulin, and metformin.

20        The compounds of formula (I) can form salts when reacted with appropriate acids or bases. Pharmaceutically acceptable salts are generally preferred over the corresponding compounds of formula (I) since they frequently produce compounds that are usually more water soluble, stable and/or more crystalline. Pharmaceutically acceptable salts are any salt which retains the activity of the parent compound and does not impart  
25        any deleterious or undesirable effect on the subject to whom it is administered and in the

context in which it is administered. Pharmaceutically acceptable salts include acid addition salts of both inorganic and organic acids. Preferred pharmaceutically acceptable salts include salts such as those described by Berge, Bighley, and Monkhouse, J. Pharm. Sci., 1977, 66, 1-19. Such salts may be formed from inorganic and organic acids.

5 Representative examples thereof include maleic, fumaric, benzoic, ascorbic, succinic, methanesulfonic, ethanedisulfonic, acetic, propionic, tartaric, salicylic, citric, gluconic, aspartic, stearic, palmitic, itaconic, glycolic, p-aminobenzoic, glutamic, benzenesulfonic, hydrochloric, hydrobromic, sulfuric, cyclohexylsulfamic, phosphoric and nitric acids. For other acceptable salts, see *Int. J. Pharm.*, 33, 201-217 (1986).

## 10 **Methods of the Invention**

The compounds of the invention, pharmaceutical formulations comprising said compounds, and pharmaceutically acceptable salts thereof, are useful for treating mammals suffering from a disease or condition characterized by at least one pathological form of abnormal HDL and/or LDL levels, triglyceride levels, and/or glucose levels in  
15 blood, and are useful for helping to prevent or delay the onset of such a condition. The compounds and formulations of the invention are particularly useful for treating, preventing, or slowing the progression of metabolic disorders, including, for example, hypercholesteremia, hypertriglyceridemia, low HDL-C atherosclerosis, hyperglycemia, syndrome X, hyperinsulinemia, and diabetes. When treating or preventing these diseases,  
20 the compounds of the invention can either be used individually or in combination, as is best for the subject.

With regard to these diseases, the term "treating" means that compounds of the invention can be used in subjects, preferably human subjects/patients, with existing disease. The compounds of the invention will not necessarily cure the subject who has the

disease but will delay or slow the progression or prevent further progression of the disease thereby giving the individual a more useful life span.

The term "preventing" means that that if the compounds of the invention are administered to those who do not now have the disease but who would normally develop the disease or be at increased risk for the disease, they will not develop the disease. In addition, "preventing" also includes delaying the development of the disease in an individual who will ultimately develop the disease or would be at risk for the disease due to age, familial history, genetic or chromosomal abnormalities, and/or due to the presence of one or more biological markers for the disease. By delaying the onset of the disease, compounds of the invention can prevent the individual from getting the disease during the period in which the individual would normally have gotten the disease or reduce the rate of development of the disease or some of its effects but for the administration of compounds of the invention up to the time the individual ultimately gets the disease. Preventing also includes administration of the compounds of the invention to those individuals thought to have predisposition for the disease.

In a preferred aspect, the compounds of the invention are useful for slowing the progression of disease symptoms.

In another preferred aspect, the compounds of the invention are useful for preventing the further progression of disease symptoms.

In treating or preventing the above diseases, the compounds of the invention are administered in a therapeutically effective amount. The therapeutically effective amount will vary depending on the particular compound used and the route of administration, as is known to those skilled in the art.

In treating a subject displaying any of the diagnosed above conditions a physician may administer a compound of the invention immediately and continue administration indefinitely, as needed.

#### **Dosage Forms and Amounts**

5           The compounds of the invention can be administered orally, parenterally, (IV, IM, depo-IM, SQ, and depo SQ), sublingually, intranasally (inhalation), intrathecally, topically, or rectally. Dosage forms known to those of skill in the art are suitable for delivery of the compounds of the invention.

10           Compositions are provided that contain therapeutically effective amounts of the compounds of the invention. The compounds are preferably formulated into suitable pharmaceutical preparations such as tablets, capsules, or elixirs for oral administration or in sterile solutions or suspensions for parenteral administration. Typically the compounds described above are formulated into pharmaceutical compositions using techniques and procedures well known in the art.

15           About 1 to 500 mg of a compound or mixture of compounds of the invention or a physiologically acceptable salt or ester is compounded with a physiologically acceptable vehicle, carrier, excipient, binder, preservative, stabilizer, flavor, etc., in a unit dosage form as called for by accepted pharmaceutical practice. The amount of active substance in those compositions or preparations is such that a suitable dosage in the range indicated  
20           is obtained. The compositions are preferably formulated in a unit dosage form, each dosage containing from about 2 to about 100 mg, more preferably about 10 to about 30 mg of the active ingredient. The term "unit dosage form" refers to physically discrete units suitable as unitary dosages for human subjects and other mammals, each unit containing a predetermined quantity of active material calculated to produce the desired  
25           therapeutic effect, in association with a suitable pharmaceutical excipient.

To prepare compositions, one or more compounds of the invention are mixed with a suitable pharmaceutically acceptable carrier. Upon mixing or addition of the compound(s), the resulting mixture may be a solution, suspension, emulsion, or the like. Liposomal suspensions may also be suitable as pharmaceutically acceptable carriers.

5 These may be prepared according to methods known to those skilled in the art. The form of the resulting mixture depends upon a number of factors, including the intended mode of administration and the solubility of the compound in the selected carrier or vehicle. The effective concentration is sufficient for lessening or ameliorating at least one symptom of the disease, disorder, or condition treated and may be empirically  
10 determined.

Pharmaceutical carriers or vehicles suitable for administration of the compounds provided herein include any such carriers known to those skilled in the art to be suitable for the particular mode of administration. In addition, the active materials can also be mixed with other active materials that do not impair the desired action, or with materials  
15 that supplement the desired action, or have another action. The compounds may be formulated as the sole pharmaceutically active ingredient in the composition or may be combined with other active ingredients.

Where the compounds exhibit insufficient solubility, methods for solubilizing may be used. Such methods are known and include, but are not limited to, using cosolvents  
20 such as dimethylsulfoxide (DMSO), using surfactants such as Tween®, and dissolution in aqueous sodium bicarbonate. Derivatives of the compounds, such as salts or prodrugs may also be used in formulating effective pharmaceutical compositions.

The concentration of the compound is effective for delivery of an amount upon administration that lessens or ameliorates at least one symptom of the disorder for which

the compound is administered. Typically, the compositions are formulated for single dosage administration.

The compounds of the invention may be prepared with carriers that protect them against rapid elimination from the body, such as time-release formulations or coatings.

5 Such carriers include controlled release formulations, such as, but not limited to, microencapsulated delivery systems. The active compound is included in the pharmaceutically acceptable carrier in an amount sufficient to exert a therapeutically useful effect in the absence of undesirable side effects on the subject treated. The therapeutically effective concentration may be determined empirically by testing the  
10 compounds in known *in vitro* and *in vivo* model systems for the treated disorder.

The compounds and compositions of the invention can be enclosed in multiple or single dose containers. The enclosed compounds and compositions can be provided in kits, for example, including component parts that can be assembled for use. For example, a compound inhibitor in lyophilized form and a suitable diluent may be provided as  
15 separated components for combination prior to use. A kit may include a compound inhibitor and a second therapeutic agent for co-administration. The inhibitor and second therapeutic agent may be provided as separate component parts. A kit may include a plurality of containers, each container holding one or more unit dose of the compound of the invention. The containers are preferably adapted for the desired mode of  
20 administration, including, but not limited to tablets, gel capsules, sustained-release capsules, and the like for oral administration; depot products, pre-filled syringes, ampoules, vials, and the like for parenteral administration; and patches, medipads, creams, and the like for topical administration.

The concentration of active compound in the drug composition will depend on absorption, inactivation, and excretion rates of the active compound, the dosage schedule, and amount administered as well as other factors known to those of skill in the art.

The active ingredient may be administered at once, or may be divided into a  
5 number of smaller doses to be administered at intervals of time. It is understood that the precise dosage and duration of treatment is a function of the disease being treated and may be determined empirically using known testing protocols or by extrapolation from *in vivo* or *in vitro* test data. It is to be noted that concentrations and dosage values may also vary with the severity of the condition to be alleviated. It is to be further understood that  
10 for any particular subject, specific dosage regimens should be adjusted over time according to the individual need and the professional judgment of the person administering or supervising the administration of the compositions, and that the concentration ranges set forth herein are exemplary only and are not intended to limit the scope or practice of the claimed compositions.

15 If oral administration is desired, the compound should be provided in a composition that protects it from the acidic environment of the stomach. For example, the composition can be formulated in an enteric coating that maintains its integrity in the stomach and releases the active compound in the intestine. The composition may also be formulated in combination with an antacid or other such ingredient.

20 Oral compositions will generally include an inert diluent or an edible carrier and may be compressed into tablets or enclosed in gelatin capsules. For the purpose of oral therapeutic administration, the active compound or compounds can be incorporated with excipients and used in the form of tablets, capsules, or troches. Pharmaceutically compatible binding agents and adjuvant materials can be included as part of the  
25 composition.



The tablets, pills, capsules, troches, and the like can contain any of the following ingredients or compounds of a similar nature: a binder such as, but not limited to, gum tragacanth, acacia, corn starch, or gelatin; an excipient such as microcrystalline cellulose, starch, or lactose; a disintegrating agent such as, but not limited to, alginic acid and corn starch; a lubricant such as, but not limited to, magnesium stearate; a gildant, such as, but not limited to, colloidal silicon dioxide; a sweetening agent such as sucrose or saccharin; and a flavoring agent such as peppermint, methyl salicylate, or fruit flavoring.

When the dosage unit form is a capsule, it can contain, in addition to material of the above type, a liquid carrier such as a fatty oil. In addition, dosage unit forms can contain various other materials, which modify the physical form of the dosage unit, for example, coatings of sugar and other enteric agents. The compounds can also be administered as a component of an elixir, suspension, syrup, wafer, chewing gum or the like. A syrup may contain, in addition to the active compounds, sucrose as a sweetening agent and certain preservatives, dyes and colorings, and flavors.

The active materials can also be mixed with other active materials that do not impair the desired action, or with materials that supplement the desired action.

Solutions or suspensions used for parenteral, intradermal, subcutaneous, or topical application can include any of the following components: a sterile diluent such as water for injection, saline solution, fixed oil, a naturally occurring vegetable oil such as sesame oil, coconut oil, peanut oil, cottonseed oil, and the like, or a synthetic fatty vehicle such as ethyl oleate, and the like, polyethylene glycol, glycerine, propylene glycol, or other synthetic solvent; antimicrobial agents such as benzyl alcohol and methyl parabens; antioxidants such as ascorbic acid and sodium bisulfite; chelating agents such as ethylenediaminetetraacetic acid (EDTA); buffers such as acetates, citrates, and phosphates; and agents for the adjustment of tonicity such as sodium chloride and

dextrose. Parenteral preparations can be enclosed in ampoules, disposable syringes, or multiple dose vials made of glass, plastic, or other suitable material. Buffers, preservatives, antioxidants, and the like can be incorporated as required.

Where administered intravenously, suitable carriers include physiological saline, phosphate buffered saline (PBS), and solutions containing thickening and solubilizing agents such as glucose, polyethylene glycol, polypropyleneglycol, and mixtures thereof. Liposomal suspensions including tissue-targeted liposomes may also be suitable as pharmaceutically acceptable carriers. These may be prepared according to methods known for example, as described in U.S. Patent No. 4,522,811.

The active compounds may be prepared with carriers that protect the compound against rapid elimination from the body, such as time-release formulations or coatings. Such carriers include controlled release formulations, such as, but not limited to, implants and microencapsulated delivery systems, and biodegradable, biocompatible polymers such as collagen, ethylene vinyl acetate, polyanhydrides, polyglycolic acid, polyorthoesters, polylactic acid, and the like. Methods for preparation of such formulations are known to those skilled in the art.

The compounds of the invention can be administered orally, parenterally (IV, IM, depo-IM, SQ, and depo-SQ), sublingually, intranasally (inhalation), intrathecally, topically, or rectally. Dosage forms known to those skilled in the art are suitable for delivery of the compounds of the invention.

Compounds of the invention may be administered enterally or parenterally. When administered orally, compounds of the invention can be administered in usual dosage forms for oral administration as is well known to those skilled in the art. These dosage forms include the usual solid unit dosage forms of tablets and capsules as well as liquid dosage forms such as solutions, suspensions, and elixirs. When the solid dosage forms

are used, it is preferred that they be of the sustained release type so that the compounds of the invention need to be administered only once or twice daily.

The oral dosage forms are administered to the subject 1, 2, 3, or 4 times daily. It is preferred that the compounds of the invention be administered either three or fewer  
5 times, more preferably once or twice daily. Hence, it is preferred that the compounds of the invention be administered in oral dosage form. It is preferred that whatever oral dosage form is used, that it be designed so as to protect the compounds of the invention from the acidic environment of the stomach. Enteric coated tablets are well known to those skilled in the art. In addition, capsules filled with small spheres each coated to  
10 protect from the acidic stomach, are also well known to those skilled in the art.

As noted above, depending on whether asymmetric carbon atoms are present, the compounds of the invention can be present as mixtures of isomers, especially as racemates, or in the form of pure isomers, especially optical antipodes.

Salts of compounds are preferably the pharmaceutically acceptable or non-toxic  
15 salts of compounds of formula I. For isolation and purification purposes it is also possible to use pharmaceutically unacceptable salts.

### **Synthesis of Compounds**

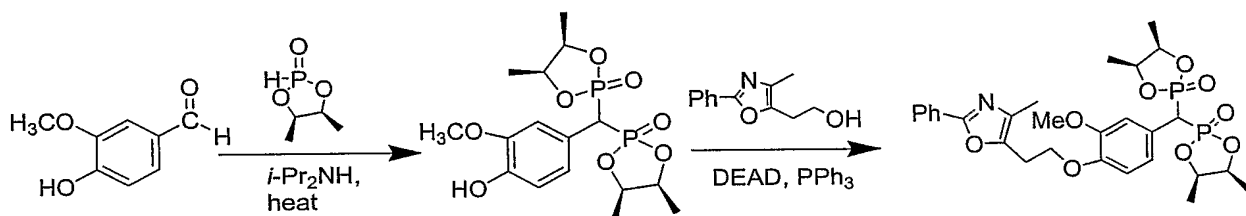
The compounds useful in the methods of the invention can be synthesized using the procedures set forth in Schemes I-VI below. Those skilled in the art will appreciate  
20 that minor modifications may be made to the specific procedures in that article to arrive at compounds useful in the invention.

Compounds of the present invention can be made by a variety of routes. The most important involve the very well characterized additions of phosphite derivatives, [Simoni et al., Tetrahedron Letters (1998), 39(41), 7615-7618.] or silylphosphite derivatives  
25 [Afarinkia et al., Tetrahedron (1990), 46(20), 7175-96.] across carbonyl double bonds, the

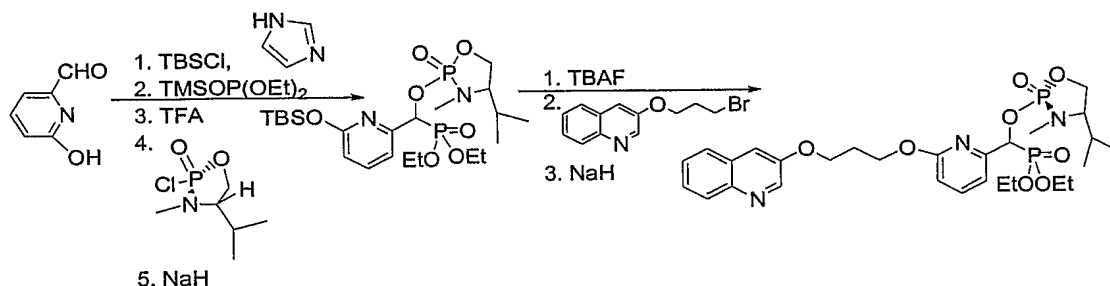
so-called Abramov reaction [Abramov, V. S.; S. M. Kirov, Doklady Akademii Nauk SSSR (1950), 73 487-9]. Variations described in the literature include additions across aldehydes, ketones, acyl chlorides, [Pohjala et al., PCT Int. Appl. (1992 WO 9211269 A1 US Patent 5,393,748], acylphosphonates, [Lecouvey et al., Heteroatom Chemistry (2000), 11(7), 556-561], amides, [Failla et al., Heteroatom Chemistry (2000), 11(7), 493-504.], and imines, [Wolfsberger, W., Chemiker-Zeitung (1985), 109(10), 317-32.]. Phosphite species, most of which are known to add across carbonyls, include diesters, cyclic esters, diamides, [Evans et al., Tetrahedron Letters (1977), (29), 2495-8.] cyclic diamides, [Pudovik et al., Izvestiya Akademii Nauk SSSR, Seriya Khimicheskaya (1980), (5), 1183-5.], and chiral cyclic phosphinamidoates, Sum, V.; Kee, T. P., Journal of the Chemical Society, Perkin Transactions 1 (1993), (22), 2701-11.], as well as thiophosphites [Pudovik, A. N.; Zametaeva, G. A. Bull. Acad. Sci. U.S.S.R., Classe sci. chim. (1952), 825-30.], phosphinites, [Yamagishi et al., Tetrahedron (2003), 59(6), 767-772.], silylaminophosphines, [Heilson, R. H.; Goebel, D. W. Journal of the Chemical Society, Chemical Communications (1979), (17), 769-70.], phosphine oxides and phosphine sulfides. [Goerlich, J. R.; Schmutzler, R. Phosphorus, Sulfur and Silicon and the Related Elements (1995), 101(1-4), 213-20.]. Similar transformations can be carried out by using trialkyl phosphite esters and  $\text{POCl}_3$ , [Olive, G.; Jacques, A., Phosphorus, Sulfur and Silicon and the Related Elements (2003), 178(1), 33-46.], or phosphorus (III) halides and acetic acid, [et al., Journal of the American Chemical Society, (1923), 45, 165-71.]. The  $\alpha$ -hydrox(bis)phosphonate derivatives obtained in several of these processes may be converted to other compounds of the invention such as the 1,1-bisphosphonates and 1-phosphatophosphonates, by methods described in the literature. 1,1-bisphosphonates may also be made from anions derived from the corresponding diphosphonylated methane derivatives, [Vepsalainen et al., Acta Chemica Scandinavica (1997), 51(9), 932-937.]

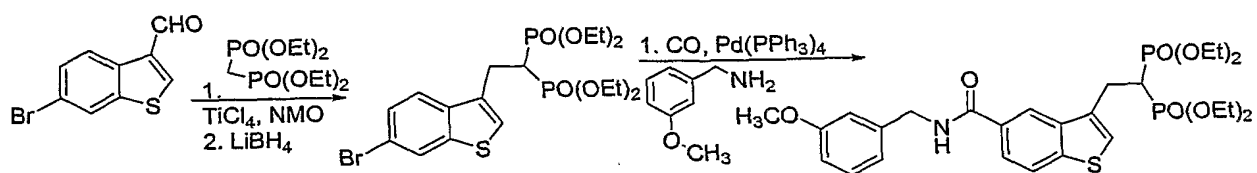
which can be alkylated [Pohjala et al., PCT Int. Appl. (1992), WO 9211269 A1 US Patent 5,393,748. Hutchinson, D. W.; Semple, G., Journal of Organometallic Chemistry (1985), 291(2), 145-51,], condensed with carbonyl compounds, [Nguyen et al., Current Medicinal Chemistry: Immunology, Endocrine & Metabolic Agents (2002), 2(3), 205-217,], or crosscoupled under transition metal catalysis [Sulsky, R.; Magnin, D. R. Synlett (1993), (12), 933-4.]. 1,2-Bisphosphonates can be made from aldehydes by Horner-Emmons reaction to produce a vinyl phosphonate, [Minami, T.; Motoyoshiya, J., Synthesis (1992), (4), 333-49. Davis et al., Tetrahedron Letters (1998), 39(35), 6263-6266,], followed by Michael addition of a second phosphite species.

### Synthetic Scheme I:

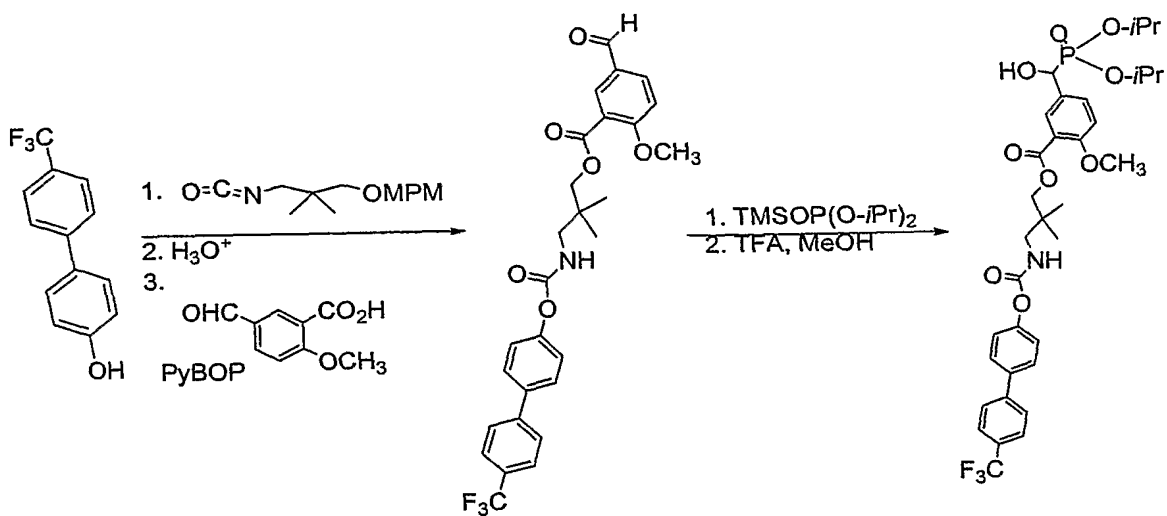


### Synthetic Scheme II:

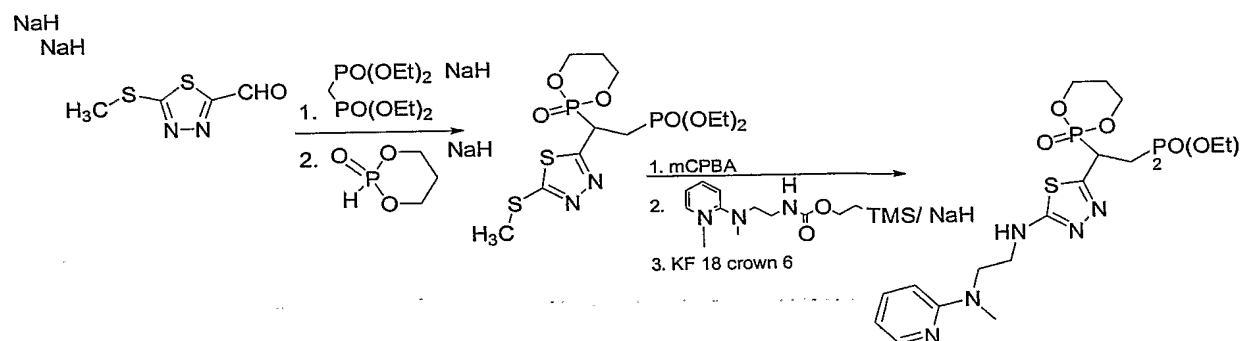


**Synthetic Scheme III:**

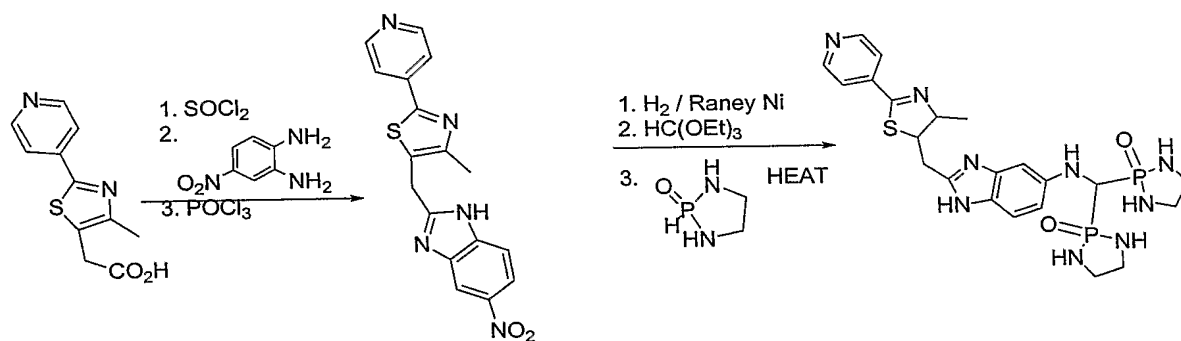
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10 **Synthetic Scheme IV:**

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**Synthetic Scheme V:**

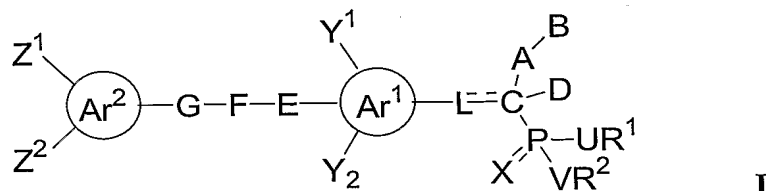
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**Synthetic Scheme VI:**

10

## WHAT IS CLAIMED IS:

1. A compound of the Formula (I):



5 wherein

A is a bond, O, CH<sub>2</sub>, CHF, CF<sub>2</sub>, or NR<sub>6</sub>;

B is H, C<sub>1</sub>-C<sub>6</sub> lower alkyl, or P(=X<sup>1</sup>)(UR<sup>3</sup>)(VR<sup>4</sup>);

D is a) H or lower alkyl, wherein the L=C bond is a single bond; or

b) OH, OCOR<sup>5</sup>, NH<sub>2</sub>, NR<sup>6</sup>R<sup>6a</sup>, or NHCOR<sup>5</sup>, wherein the L=C bond is a single bond, with the proviso that A is CH<sub>2</sub>, CHF, CF<sub>2</sub>;

L is a) NR<sup>6</sup>, CR<sup>7</sup>R<sup>8</sup>, -OCR<sup>7</sup>R<sup>8</sup>-, -NR<sup>6</sup>CR<sup>7</sup>R<sup>8</sup>-, or -S(O)<sub>m</sub>CR<sup>7</sup>R<sup>8</sup>-, wherein the L=C bond is a single bond; or

b) CR<sup>7</sup>, wherein the L=C bond is a double bond, with the proviso that D is absent when the L=C bond is a double bond; or

c) absent, wherein C is covalently bonded by a single bond to Ar<sup>1</sup>;

Ar<sup>1</sup> and Ar<sup>2</sup> are each independently mono- or bicyclic aromatic rings of 5-12 atoms, including, but not limited to phenyl, pyridyl, pyrimidyl, pyrazinyl, pyridazinyl, thienyl, furanyl, pyrrolyl, imidazyl, pyrazolyl, oxazolyl, isoxoazolyl, thiazolyl, isothiazolyl, 1,3,4-oxadiazolyl, 1,2,4-oxadiazolyl, 1,3,4-thiadiazolyl, 1,2,3-triazolyl, 1,3,4-triazolyl, 1,2,4-triazinyl, 1,3,5-triazinyl, benzofuranyl, benzothienyl, indolyl, indazolyl, benzimidazyl, benzoxazolyl, benzoisoxazolyl,



benzothiazoyl, benzoisothiazolyl, quinolinyl, isoquinolinyl, quinazolinyl, quinoxalinyl, naphthyridyl, or purinyl;

$Y^1$ ,  $Y^2$ , and  $Z^1$  are each independently a lone electron pair, H, C<sub>1</sub>-C<sub>6</sub> lower alkyl, C<sub>2</sub>-C<sub>6</sub> lower alkenyl, C<sub>2</sub>-C<sub>6</sub> lower alkynyl, C<sub>1</sub>-C<sub>6</sub> lower alkoxy, C<sub>1</sub>-C<sub>6</sub> lower alkylamino, C<sub>1</sub>-C<sub>6</sub> lower dialkylamino, C<sub>2</sub>-C<sub>6</sub> lower cycloalkyl, C<sub>4</sub>-C<sub>6</sub> lower cycloalkenyl, C<sub>1</sub>-C<sub>6</sub> lower thioalkyl, C<sub>1</sub>-C<sub>6</sub> lower sulfinylalkyl, C<sub>1</sub>-C<sub>6</sub> lower sulfonylalkyl, C<sub>1</sub>-C<sub>6</sub> lower acyloxy, C<sub>1</sub>-C<sub>6</sub> lower acylamino with N substituted with R<sup>6</sup>, CH<sub>2</sub>OR<sup>5</sup>, CH<sub>2</sub>NR<sup>6</sup>R<sup>6a</sup>, R<sub>f</sub>, R<sub>f</sub>O, OH, NH<sub>2</sub>, CN, NO<sub>2</sub>, F, Cl, Br, I, or N<sub>3</sub>;

E is a bond, S(O)<sub>m</sub>, NR<sup>6</sup>, C=O, CO<sub>2</sub>, CONR<sup>6</sup>, O, -OC=O, NR<sup>6</sup>C=O, NR<sup>6</sup>CO<sub>2</sub>, OC=ONR<sup>6</sup>, OCO<sub>2</sub>, or NR<sup>6</sup>CONR<sup>6a</sup>;

F is (CH<sub>2</sub>)<sub>n</sub>, (CH<sub>2</sub>)<sub>o</sub>O(CH<sub>2</sub>)<sub>p</sub>, (CH<sub>2</sub>)<sub>o</sub>NR<sup>6</sup>(CH<sub>2</sub>)<sub>p</sub>, (CH<sub>2</sub>)<sub>o</sub>NR<sup>6</sup>CO(CH<sub>2</sub>)<sub>p</sub>, (CH<sub>2</sub>)<sub>o</sub>CONR<sup>6</sup>(CH<sub>2</sub>)<sub>p</sub>, (CH<sub>2</sub>)<sub>o</sub>(CR<sup>6</sup>=CR<sup>6</sup>)<sub>q</sub>(CH<sub>2</sub>)<sub>p</sub>, (CH<sub>2</sub>)<sub>o</sub>-(C≡C)<sub>q</sub>-(CH<sub>2</sub>)<sub>p</sub>;

G is a bond, O, NR<sup>6</sup>, CO, CO<sub>2</sub>, OCO, OCO<sub>2</sub>, S(O)<sub>m</sub>, CONR<sup>6</sup>, NR<sup>6</sup>CO, NR<sup>6</sup>CO<sub>2</sub>, OCONR<sup>6</sup>, NR<sup>6</sup>CONR<sup>6a</sup>, or G can optionally be attached to Ar<sup>2</sup> at two contiguous C atoms to form a 5- to 7-membered partially saturated ring, which contains 0, 1, or 2 heteroatoms selected from the group consisting of O, N, and S;

X, X<sup>1</sup> are independently O or S

Z<sup>2</sup> is nothing, H or Ar<sup>1</sup> optionally substituted with Y<sup>1</sup> and Y<sup>2</sup>;

R<sup>1</sup>, R<sup>2</sup>, R<sup>3</sup>, and R<sup>4</sup>, are each independently selected from H, C<sub>1</sub>-C<sub>6</sub> lower alkyl, C<sub>3</sub>-C<sub>6</sub> lower alkenyl, C<sub>3</sub>-C<sub>6</sub> lower alkynyl, C<sub>3</sub>-C<sub>6</sub> lower cycloalkyl, C<sub>4</sub>-C<sub>6</sub> lower cycloalkenyl, or independently R<sup>1</sup> and R<sup>2</sup> or R<sup>3</sup> and R<sup>4</sup> can be taken together to form a 5 to 8-membered ring containing 2-7 carbon atoms, the 5 to 8-membered ring optionally substituted with zero to 3 substituents selected from the group C<sub>1</sub>-C<sub>4</sub> lower alkyl, C<sub>1</sub>-C<sub>4</sub> lower alkoxy, C<sub>1</sub>-C<sub>4</sub> lower alkylamino, C<sub>1</sub>-C<sub>4</sub> lower

dialkylamino, amino, hydroxyl, hydroxymethyl, methoxymethyl, phenyl, substituted phenyl, benzyl, substituted benzyl;

U and V are each independently a bond, O or  $\text{NR}^6$ ;

$\text{R}^5$ ,  $\text{R}^6$  and  $\text{R}^{6a}$  are each independently  $\text{C}_1$ - $\text{C}_6$  alkyl,  $\text{C}_3$ - $\text{C}_6$  cycloalkyl,  $\text{C}_3$ - $\text{C}_6$  alkenyl,  $\text{C}_3$ - $\text{C}_6$  cycloalkenyl,  $\text{C}_3$ - $\text{C}_6$  alkynyl, and H;

$\text{R}^7$  and  $\text{R}^8$  are each independently H,  $\text{C}_1$ - $\text{C}_4$  lower alkyl, or are taken together to form a saturated  $\text{C}_3$ - $\text{C}_6$  carbocyclic ring;

$\text{R}_f$  is  $\text{C}_1$ - $\text{C}_4$  straight or branched lower perfluoroalkyl;

all lower alkyl, alkenyl and alkynyl groups including those linked via heteroatoms can be straight chain or branched;

m is 0, 1, or 2;

n is 0, 1, 2, 3, 4, 5, or 6;

o is 0, 1, 2, 3, 4, 5, or 6;

p is 0, 1, 2, 3, 4, 5, or 6; and

q is 0, 1, 2, 3, 4, 5, or 6;

with the provisos that

when A is a bond or O, B is  $\text{P}(\text{O})(\text{OR}^3)(\text{OR}^4)$ , and D is selected from the group H, OH,  $\text{OCOCH}_3$ , and  $\text{NH}_2$ , and when  $\text{R}^1 = \text{R}^2$  and  $\text{R}^3 = \text{R}^4$ , and both are selected from the group H or unsubstituted  $\text{C}_1$ - $\text{C}_4$  lower alkyl, and E and G are bonds, and F is  $(\text{CH}_2)_n$  where n is 0, and both  $\text{Ar}^1$  and  $\text{Ar}^2$  are phenyl, then at least one of  $\text{Y}^1$ ,  $\text{Y}^2$ ,  $\text{Z}^1$ , or  $\text{Z}^2$  must not be H; and

when A is a bond or  $\text{CH}_2$ , and B is  $\text{P}(\text{O})(\text{OR}^3)(\text{OR}^4)$ , and either D is H or  $\text{C}_1$ - $\text{C}_4$  lower alkyl where L is  $\text{CH}_2$ , or D is absent, with  $\text{L}=\text{C}$  taken together represent an ethenylidene group, and  $\text{Ar}^1$  is phenyl, and E is a bond or O, and  $\text{R}^1 = \text{R}^2$  and  $\text{R}^3 = \text{R}^4$ , and both are drawn from the group H or  $\text{C}_1$ - $\text{C}_6$  unsubstituted lower alkyl, then one of

$Y^1$  and  $Y^2$  must be other than H or unsubstituted  $C_1$ - $C_4$  lower alkyl or unsubstituted  $C_1$ - $C_4$  lower alkoxy; and

when A is O, and B is H or  $P(O)(OR^3)(OR^4)$ , and  $R^1$ ,  $R^2$ ,  $R^3$ , and  $R^4$  are all selected from the group H or  $C_1$ - $C_6$  unsubstituted lower alkyl, and D is H, and L is a bond, and  $Ar^1$  is phenyl, and E is other than a bond or O, then one of  $Y^1$  or  $Y^2$  must be other than H, or  $C_1$ - $C_4$  unsubstituted lower alkyl or  $C_1$ - $C_4$  unsubstituted lower alkoxy.

2. The compound according to Claim 1, wherein

10 A is selected from a bond, O, and  $CH_2$ ;

B is  $P(=O)(UR^3)(VR^4)$ ;

D is H; and

the  $L \equiv C$  bond is a single bond.

15 3. A compound according to Claim 2, wherein  $Ar^1$  is phenyl.

4. A compound according to Claim 3, wherein U and V are each O.

20 5. A compound according to Claim 1, wherein the compound is selected from the group consisting of:

Diethyl 1-(diethoxyphosphinyloxy)-1-(4-[2-{*N*-methyl-*N*-pyrid-2-ylamino}ethoxy]-3-fluorophenyl)methylphosphonate;

Diethyl 1-(diethoxyphosphinyloxy)-1-(4-[N-(2-{*N*-methyl-*N*-pyrid-2-ylamino}ethyl)-*N*-methylaminocarbonyl]-3-fluorophenyl)methylphosphonate;

- Diethyl 1-(diethoxyphosphinyloxy)-1-(4-[3-{*N*-methyl-*N*-pyrid-2-ylamino}-1-oxoprop-1-yl]-3-fluorophenyl)methylphosphonate;
- Diethyl 1-(diethoxyphosphinyloxy)-1-(4-[2-{5-methyl-2-phenyloxazol-4-yl}ethoxy]-3-fluorophenyl)methylphosphonate;
- 5 Diethyl 1-(diethoxyphosphinyloxy)-1-(4-[*N*-(2-{5-methyl-2-phenyloxazol-4-yl}ethyl)-*N*-methylaminocarbonyl]-3-fluorophenyl)methylphosphonate;
- Diethyl 1-(diethoxyphosphinyloxy)-1-(4-[2-{5-methyl-2-phenylthiazol-4-yl}ethoxy]-3-fluorophenyl)methylphosphonate;
- Diethyl 1-(diethoxyphosphinyloxy)-1-(4-[3-{5-methyl-2-phenylthiazol-4-yl}-1-oxoprop-1-yl]-3-fluorophenyl)methylphosphonate;
- 10 Diethyl 1-(diethoxyphosphinyloxy)-1-(4-[2-{5-methyl-2-pyrid-4-yloxazol-4-yl}ethoxy]-3-fluorophenyl)methylphosphonate;
- Diethyl 1-(diethoxyphosphinyloxy)-1-(4-[2-{5-methyl-2-pyrid-4-ylthiazol-4-yl}ethoxy]-3-fluorophenyl)methylphosphonate;
- 15 Diethyl 1-(diethoxyphosphinyloxy)-1-(4-[3-{5-methyl-2-pyrid-4-yloxazol-4-yl}-1-oxoprop-1-yl]-3-fluorophenyl)methylphosphonate;
- Diethyl 1-(hydroxy)-1-(4-[*N*-(2-{5-methyl-2-pyrid-4-ylthiazol-4-yl}ethyl)-*N*-methylaminocarbonyl]-3-fluorophenyl)methylphosphonate;
- Diethyl 1-(hydroxy)-1-(4-[2-{4-(4-trifluoromethylphenyl)phenoxy}ethoxy]-3-fluorophenyl)methylphosphonate;
- 20 Diethyl 1-(hydroxy)-1-(4-[*N*-(2-{4-(4-trifluoromethylphenyl)phenoxy}ethyl)-*N*-methylaminocarbonyl]-3-fluorophenyl)methylphosphonate;
- Diethyl 1-(hydroxy)-1-(4-[3-{4-(4-trifluoromethylphenyl)phenoxy}-1-oxoprop-1-yl]-3-fluorophenyl)methylphosphonate;

- Diethyl 1-(hydroxy)-1-(4-[2-{1-[4-(2-trifluoromethylphenyl)phenylmethyl]-3-hexylureido}ethyl]-3-fluorophenyl)methylphosphonate;
- Diethyl 1-(hydroxy)-1-(4-[2-{1-butyl-3-(5-methoxypyrid-2-yl)ureido}ethyl]-3-fluorophenyl)methylphosphonate;
- 5 Diethyl 1-(hydroxy)-1-(4-[3-{4-acetyl-3-hydroxy-2-propylphenoxy}propoxy]-3-fluorophenyl)methylphosphonate;
- Diethyl 1-(hydroxy)-1-(4-[2-{4*H*-3-oxobenzo[1,4]oxazin-2-yl}ethoxy]-3-fluorophenyl)methylphosphonate;
- Diethyl 1-(hydroxy)-1-(4-[3,*N*-phthalimidopropoxy]-3-
- 10 fluorophenyl)methylphosphonate;
- Diethyl 1-(hydroxy)-1-(4-[4,*N*-phthalimidobutoxy]-3-fluorophenyl)methylphosphonate;
- Tetraethyl 1-(3-[3-{*N*-methyl-*N*-pyrid-2-ylamino}propoxy]-4-fluorophenyl)methylidenebisphosphonate;
- 15 Tetraethyl 1-(3-[*N*-(3-{*N*-methyl-*N*-pyrid-2-ylamino}propyl)-*N*-methylamino]-4-fluorophenyl)methylidenebisphosphonate;
- Tetraethyl 1-(3-[3-{*N*-methyl-*N*-pyrid-2-ylamino}-1-oxoprop-1-ylamino]-4-fluorophenyl)methylidenebisphosphonate;
- Tetraethyl 1-(3-[3-{5-methyl-2-phenyloxazol-4-yl}propoxy]-4-
- 20 fluorophenyl)methylidenebisphosphonate;
- Tetraethyl 1-(3-[*N*-(2-{5-methyl-2-phenyloxazol-4-yl}ethyl)-*N*-methylaminocarbonyl]-4-methoxyphenyl)methylidenebisphosphonate;
- Tetraethyl 1-(3-[3-{5-methyl-2-phenylthiazol-4-yl}propoxy]-4-fluorophenyl)methylidenebisphosphonate;

- Tetraethyl 1-(3-[3-{5-methyl-2-phenylthiazol-4-yl}-1-oxoprop-1-yl]-4-fluorophenyl)methylidenebisphosphonate;
- Tetraethyl 1-(3-[4-{5-methyl-2-pyrid-4-yloxazol-4-yl}butoxy]-4-fluorophenyl)methylidenebisphosphonate;
- 5 Tetraethyl 1-(3-[3-{5-methyl-2-pyrid-4-ylthiazol-4-yl}propoxy]-4-fluorophenyl)methylidenebisphosphonate;
- Tetraethyl 1-(3-[3-{5-methyl-2-pyrid-4-yloxazol-4-yl}-1-oxoprop-1-ylthio]-4-fluorophenyl)methylidenebisphosphonate;
- Tetraethyl 2-(3-[*N*-(3-{5-methyl-2-pyrid-4-ylthiazol-4-yl}propyl)-*N*-methylamino]-4-fluorophenyl)vinylidene-1,1-bisphosphonate;
- 10 Tetraethyl 2-(3-[3-{4-(4-trifluoromethylphenyl)phenoxy}propoxy]-4-fluorophenyl)vinylidene-1,1-bisphosphonate;
- Tetraethyl 2-(3-[*N*-(3-{4-(4-trifluoromethylphenyl)phenoxy}propyl)-*N*-methylamino]-4-fluorophenyl)vinylidene-1,1-bisphosphonate;
- 15 Tetraethyl 2-(3-[4-{4-(4-trifluoromethylphenyl)phenoxy}-1-oxobut-1-yl]-4-fluorophenyl)vinylidene-1,1-bisphosphonate;
- Tetraethyl 2-(3-[2-{1-[4-(2-trifluoromethylphenyl)phenylmethyl]-3-hexylureido}ethyl]-4-fluorophenyl)vinylidene-1,1-bisphosphonate;
- Tetraethyl 2-(3-[2-{1-butyl-3-(5-methoxypyrid-2-yl)ureido}ethyl]-4-fluorophenyl)vinylidene-1,1-bisphosphonate;
- 20 Tetraethyl 2-(3-[4-{4-acetyl-3-hydroxy-2-propylphenoxy}butoxy]-4-fluorophenyl)vinylidene-1,1-bisphosphonate;
- Tetraethyl 2-(3-[3-{4*H*-3-oxobenzo[1,4]oxazin-2-yl}propoxy]-4-fluorophenyl)vinylidene-1,1-bisphosphonate;

- Tetraethyl 2-(3-[3,*N*-phthalimidopropoxy]-4-fluorophenyl)vinylidene-1,1-bisphosphonate;
- Tetraethyl 2-(3-[4,*N*-phthalimidobutoxy]-4-fluorophenyl)vinylidene-1,1-bisphosphonate;
- 5 Tetraethyl 1-(6-[2-{*N*-methyl-*N*-pyrid-2-ylamino}ethoxy]indol-2-yl)ethylidene-1,2-bisphosphonate;
- Tetraethyl 1-(6-[*N*-(2-{*N*-methyl-*N*-pyrid-2-ylamino}ethyl)-*N*-methylanino]indol-2-yl)ethylidene-1,2-bisphosphonate;
- Tetraethyl 1-(6-[3-{*N*-methyl-*N*-pyrid-2-ylamino}-1-oxoprop-1-yl]indol-2-yl)ethylidene-1,2-bisphosphonate;
- 10 Tetraethyl 1-(6-[2-{5-methyl-2-phenyloxazol-4-yl}ethoxy] indol-2-yl)ethylidene-1,2-bisphosphonate;
- Tetraethyl 1-(6-[*N*-(2-{5-methyl-2-phenyloxazol-4-yl}ethyl)-*N*-methylanino] indol-2-yl)ethylidene-1,2-bisphosphonate;
- 15 Tetraethyl 1-(6-[2-{5-methyl-2-phenylthiazol-4-yl}ethoxy]indol-2-yl)ethylidene-1,2-bisphosphonate;
- Tetraethyl 1-(6-[3-{5-methyl-2-phenylthiazol-4-yl}-1-oxoprop-1-yl]indol-2-yl)ethylidene-1,2-bisphosphonate;
- Tetraethyl 1-(6-[2-{5-methyl-2-pyrid-4-yloxazol-4-yl}ethoxy]indol-2-yl)ethylidene-1,2-bisphosphonate;
- 20 Tetraethyl 1-(6-[2-{5-methyl-2-pyrid-4-ylthiazol-4-yl}ethoxy]indol-2-yl)ethylidene-1,2-bisphosphonate;
- Tetraethyl 1-(6-[3-{5-methyl-2-pyrid-4-yloxazol-4-yl}-1-oxoprop-1-yl]indol-2-yl)ethylidene-1,2-bisphosphonate;

- Tetraethyl 2-(6-[*N*-(2-{5-methyl-2-pyrid-4-ylthiazol-4-yl}ethyl)-*N*-methylamino]indol-2-yl)ethylidene-1,1-bisphosphonate;
- Tetraethyl 2-(6-[2-{4-(4-trifluoromethylphenyl)phenoxy}ethoxy] indol-2-yl)ethylidene-1,1-bisphosphonate;
- 5     Tetraethyl 2-(6-[*N*-(2-{4-(4-trifluoromethylphenyl)phenoxy}ethyl)-*N*-methylamino]indol-2-yl)ethylidene-1,1-bisphosphonate;
- Tetraethyl 2-(6-[2-{1-[4-(2-trifluoromethylphenyl)phenylmethyl]-3-hexylureido}ethyl]indol-2-yl)ethylidene-1,1-bisphosphonate;
- Tetraethyl 2-(6-[2-{1-butyl-3-(5-methoxypyrid-2-yl)ureido}ethyl]indol-2-yl)ethylidene-1,1-bisphosphonate;
- 10     Tetraethyl 2-(6-[3-{4-(4-trifluoromethylphenyl)phenoxy}-1-oxoprop-1-yl]indol-2-yl)ethylidene-1,1-bisphosphonate;
- Tetraethyl 2-(6-[3-{4-acetyl-3-hydroxy-2-propylphenoxy}propoxy]indol-2-yl)ethylidene-1,1-bisphosphonate;
- 15     Tetraethyl 2-(6-[2-{4*H*-3-oxobenzo[1,4]oxazin-2-yl}ethoxy]indol-2-yl)ethylidene-1,1-bisphosphonate;
- Tetraethyl 2-(6-[3,*N*-phthalimidopropoxy]indol-2-yl)ethylidene-1,1-bisphosphonate;
- Tetraethyl 2-(6-[4,*N*-phthalimidobutoxy]indol-2-yl)ethylidene-1,1-bisphosphonate;
- Tetraethyl *N*-(5-[2-{*N*-methyl-*N*-pyrid-2-ylamino}ethoxy]pyrid-2-yl)aminomethylidenebisphosphonate;
- 20     Tetraethyl *N*-(5-[*N*-(2-{*N*-methyl-*N*-pyrid-2-ylamino}ethyl)-*N*-methylamino]pyrid-2-yl)aminomethylidenebisphosphonate;
- Tetraethyl *N*-(5-[3-{*N*-methyl-*N*-pyrid-2-ylamino}-1-oxoprop-1-yl]pyrid-2-yl)aminomethylidenebisphosphonate;



- Tetraethyl *N*-(5-[2-{5-methyl-2-phenyloxazol-4-yl}ethoxy]pyrid-2-yl)aminomethylidenebisphosphonate
- Tetraethyl *N*-(5-[*N*-(2-{5-methyl-2-phenyloxazol-4-yl}ethyl)-*N*-methylamino]pyrid-2-yl)aminomethylidenebisphosphonate;
- 5 Tetraethyl *N*-(5-[2-{5-methyl-2-phenylthiazol-4-yl}ethoxy]pyrid-2-yl)aminomethylidenebisphosphonate;
- Tetraethyl *N*-(5-[3-{5-methyl-2-pyrid-4-yloxazol-4-yl}-1-oxoprop-1-yl]pyrid-2-yl)aminomethylidenebisphosphonate;
- Tetraethyl *N*-(5-[*N*-(2-{5-methyl-2-pyrid-4-ylthiazol-4-yl}ethyl)-*N*-methylamino]pyrid-2-yl)aminomethylidenebisphosphonate;
- 10 Tetraethyl *N*-(5-[2-{5-methyl-2-pyrid-4-yloxazol-4-yl}ethoxy]pyrid-2-yl)aminomethylidenebisphosphonate;
- Tetraethyl *N*-(5-[2-{5-methyl-2-pyrid-4-ylthiazol-4-yl}ethoxy]pyrid-2-yl)aminomethylidenebisphosphonate;
- 15 2-[1-Hydroxy-1-(5-[*N*-(2-{5-methyl-2-pyrid-4-ylthiazol-4-yl}ethyl)-*N*-methylamino]pyrid-2-yl)methyl]-1,3,2-dioxaphospholane-2-oxide;
- 2-[1-Hydroxy-1-(5-[2-{4-(4-trifluoromethylphenyl)phenoxy}ethoxy]-pyrid-2-yl)methyl]-1,3,2-dioxaphospholane-2-oxide;
- 2-[1-Hydroxy-1-(5-[*N*-(2-{4-(4-trifluoromethylphenyl)phenoxy}ethyl)-*N*-methylamino]pyrid-2-yl)methyl]-1,3,2-dioxaphospholane-2-oxide;
- 20 2-[1-Hydroxy-1-(5-[3-{4-(4-trifluoromethylphenyl)phenoxy}-1-oxoprop-1-yl]-pyrid-2-yl)methyl]-1,3,2-dioxaphospholane-2-oxide;
- 2-[1-Hydroxy-1-(5-[2-{1-[4-(2-trifluoromethylphenyl)phenylmethyl]-3-hexylureido}ethyl]pyrid-2-yl)methyl]-1,3,2-dioxaphospholane-2-oxide;

- 2-[1-Hydroxy-1-(5-[2-{1-butyl-3-(5-methoxypyrid-2-yl)ureido}ethyl]pyrid-2-ylmethyl)-1,3,2-dioxaphospholane-2-oxide;
- 2-[1-Hydroxy-1-(5-[3-{4-acetyl-3-hydroxy-2-propylphenoxy}propoxy]pyrid-2-ylmethyl)-1,3,2-dioxaphospholane-2-oxide;
- 5 2-[1-Hydroxy-1-(5-[2-{4*H*-3-oxobenzo[1,4]oxazin-2-yl}ethoxy]pyrid-2-yl)methyl]-1,3,2-dioxaphospholane-2-oxide;
- 2-[1-Hydroxy-1-(5-[3,*N*-phthalimidopropoxy]pyrid-2-yl)methyl]-1,3,2-dioxaphospholane-2-oxide;
- 2-[1-Hydroxy-1-(5-[4,*N*-phthalimidobutoxy]pyrid-2-yl)methyl]-1,3,2-dioxaphospholane-2-oxide;
- 10 2-[1-Hydroxy-1-(5-[2-{*N*-methyl-*N*-pyrid-2-ylamino}ethoxy]benzothien-2-yl)methyl]-[4*R*]-methyl-1,3,2-dioxaphospholane-2-oxide;
- 2-[1-Hydroxy-1-(5-[*N*-(2-{*N*-methyl-*N*-pyrid-2-ylamino}ethyl)-*N*-methylamino]benzothien-2-yl)methyl]-[4*R*]-methyl-1,3,2-dioxaphospholane-2-oxide;
- 15 2-[1-Hydroxy-1-(5-[3-{*N*-methyl-*N*-pyrid-2-ylamino}-1-oxoprop-1-yl]benzothien-2-yl)methyl]-[4*R*]-methyl-1,3,2-dioxaphospholane-2-oxide;
- 2-[1-Hydroxy-1-(5-[2-{5-methyl-2-phenyloxazol-4-yl}ethoxy]benzothien-2-yl)methyl]-[4*R*]-methyl-1,3,2-dioxaphospholane-2-oxide;
- 20 2-[1-Hydroxy-1-(5-[*N*-(2-{5-methyl-2-phenyloxazol-4-yl}ethyl)-*N*-methylamino]benzothien-2-yl)methyl]-[4*R*]-methyl-1,3,2-dioxaphospholane-2-oxide;
- 2-[1-Hydroxy-1-(5-[2-{5-methyl-2-phenylthiazol-4-yl}ethoxy]benzothien-2-yl)methyl]-[4*R*]-methyl-1,3,2-dioxaphospholane-2-oxide;

- 2-[1-Hydroxy-1-(5-[3-{5-methyl-2-phenylthiazol-4-yl}-1-oxoprop-1-yl]benzothien-2-yl)methyl]- [4R]-methyl-1,3,2-dioxaphospholane-2-oxide;
- 2-[1-Hydroxy-1-(5-[2-{5-methyl-2-pyrid-4-yloxazol-4-yl}ethoxy]benzothien-2-yl)methyl]- [4R]-methyl-1,3,2-dioxaphospholane-2-oxide;
- 5 2-[1-Hydroxy-1-(5-[2-{5-methyl-2-pyrid-4-ylthiazol-4-yl}ethoxy]benzothien-2-yl)methyl]- [4R]-methyl-1,3,2-dioxaphospholane-2-oxide;
- 2-[1-Hydroxy-1-(5-[3-{5-methyl-2-pyrid-4-yloxazol-4-yl}-1-oxoprop-1-yl]benzothien-2-yl)methyl]- [4R]-methyl-1,3,2-dioxaphospholane-2-oxide;
- 2-[1-Hydroxy-1-(5-[*N*-(2-{5-methyl-2-pyrid-4-ylthiazol-4-yl}ethyl)-*N*-methylamino]benzothien-2-yl)methyl]- [4S]-methyl-1,3,2-dioxaphospholane-2-oxide;
- 10 2-[1-Hydroxy-1-(5-[2-{4-(4-trifluoromethylphenyl)phenoxy}ethoxy]benzothien-2-yl)methyl]- [4S]-methyl-1,3,2-dioxaphospholane-2-oxide;
- 2-[1-Hydroxy-1-(5-[*N*-(2-{4-(4-trifluoromethylphenyl)phenoxy}ethyl)-*N*-methylamino]benzothien-2-yl)methyl]- [4S]-methyl-1,3,2-dioxaphospholane-2-oxide;
- 15 2-[1-Hydroxy-1-(5-[3-{4-(4-trifluoromethylphenyl)phenoxy}-1-oxoprop-1-yl]benzothien-2-yl)methyl]- [4S]-methyl-1,3,2-dioxaphospholane-2-oxide;
- 2-[1-Hydroxy-1-(5-[2-{1-[4-(2-trifluoromethylphenyl)phenylmethyl]-3-hexylureido}ethyl]benzothien-2-yl)methyl]- [4S]-methyl-1,3,2-dioxaphospholane-2-oxide;
- 20 2-[1-Hydroxy-1-(5-[2-{1-butyl-3-(5-methoxypyrid-2-yl)ureido}ethyl]benzothien-2-yl)methyl]- [4S]-methyl-1,3,2-dioxaphospholane-2-oxide;
- 2-[1-Hydroxy-1-(5-[3-{4-acetyl-3-hydroxy-2-propylphenoxy}propoxy]benzothien-2-yl)methyl]- [4S]-methyl-1,3,2-dioxaphospholane-2-oxide;
- 25

- 2-[1-Hydroxy-1-(5-[2-{4*H*-3-oxobenzo[1,4]oxazin-2-yl}ethoxy]benzothien-2-yl)methyl]- [4*S*]-methyl-1,3,2-dioxaphospholane-2-oxide;
- 2-[1-Hydroxy-1-(5-[3,*N*-phthalimidopropoxy]benzothien-2-yl)methyl]- [4*S*]-methyl-1,3,2-dioxaphospholane-2-oxide;
- 5 2-[1-Hydroxy-1-(5-[4,*N*-phthalimidobutoxy]benzothien-2-yl)methyl]- [4*S*]-methyl-1,3,2-dioxaphospholane-2-oxide;
- 2-[1-Hydroxy-1-(4-[2-{*N*-methyl-*N*-pyrid-2-ylamino}ethoxy]thiazol-2-yl)methyl]-4,5-dimethyl-1,3,2-dioxaphospholane-2-oxide;
- 2-[1-Hydroxy-1-(4-[*N*-(2-{*N*-methyl-*N*-pyrid-2-ylamino}ethyl)-*N*-methylamino]thiazol-2-yl)methyl]-4,5-dimethyl-1,3,2-dioxaphospholane-2-oxide;
- 10 2-[1-Hydroxy-1-(4-[3-{*N*-methyl-*N*-pyrid-2-ylamino}-1-oxoprop-1-yl]thiazol-2-yl)methyl]-4,5-dimethyl-1,3,2-dioxaphospholane-2-oxide;
- 2-[1-Hydroxy-1-(4-[2-{5-methyl-2-phenyloxazol-4-yl}ethoxy]thiazol-2-yl)methyl]-4,5-dimethyl-1,3,2-dioxaphospholane-2-oxide;
- 15 2-[1-Hydroxy-1-(4-[*N*-(2-{5-methyl-2-phenyloxazol-4-yl}ethyl)-*N*-methylamino]thiazol-2-yl)methyl]-4,5-dimethyl-1,3,2-dioxaphospholane-2-oxide;
- 2-[1-Hydroxy-1-(4-[2-{5-methyl-2-phenylthiazol-4-yl}ethoxy]thiazol-2-yl)methyl]-4,5-dimethyl-1,3,2-dioxaphospholane-2-oxide;
- 2-[1-Hydroxy-1-(4-[3-{5-methyl-2-phenylthiazol-4-yl}-1-oxoprop-1-yl]thiazol-2-yl)methyl]-4,5-dimethyl-1,3,2-dioxaphospholane-2-oxide;
- 20 2-[1-Hydroxy-1-(4-[2-{5-methyl-2-pyrid-4-ylthiazol-4-yl}ethoxy]thiazol-2-yl)methyl]-4,5-dimethyl-1,3,2-dioxaphospholane-2-oxide;
- 2-[1-Hydroxy-1-(4-[2-{5-methyl-2-pyrid-4-ylthiazol-4-yl}ethoxy]thiazol-2-yl)methyl]-4,5-dimethyl-1,3,2-dioxaphospholane-2-oxide;

- 2-[1-Hydroxy-1-(4-[3-{5-methyl-2-pyrid-4-yloxazol-4-yl}-1-oxoprop-1-yl]thiazol-2-yl)methyl]-4,5-dimethyl-1,3,2-dioxaphospholane-2-oxide;
- 2-[1-Hydroxy-1-(4-[*N*-(2-{5-methyl-2-pyrid-4-ylthiazol-4-yl}ethyl)-*N*-methylamino]thiazol-2-yl)methyl]-1,3,2-dioxaphosphinane-2-oxide;
- 5 2-[1-Hydroxy-1-(4-[2-{4-(4-trifluoromethylphenyl)phenoxy}ethoxy]thiazol-2-yl)methyl]-1,3,2-dioxaphosphinane-2-oxide;
- 2-[1-Hydroxy-1-(4-[*N*-(2-{4-(4-trifluoromethylphenyl)phenoxy}ethyl)-*N*-methylamino]thiazol-2-yl)methyl]-1,3,2-dioxaphosphinane-2-oxide;
- 10 2-[1-Hydroxy-1-(4-[3-{4-(4-trifluoromethylphenyl)phenoxy}-1-oxoprop-1-yl]thiazol-2-yl)methyl]-1,3,2-dioxaphosphinane-2-oxide;
- 2-[1-Hydroxy-1-(4-[2-{1-[4-(2-trifluoromethylphenyl)phenylmethyl]-3-hexylureido}ethyl]thiazol-2-yl)methyl]-1,3,2-dioxaphosphinane-2-oxide;
- 2-[1-Hydroxy-1-(4-[2-{1-butyl-3-(5-methoxypyrid-2-yl)ureido}ethyl]thiazol-2-yl)methyl]-1,3,2-dioxaphosphinane-2-oxide;
- 15 2-[1-Hydroxy-1-(4-[3-{4-acetyl-3-hydroxy-2-propylphenoxy}propoxy]thiazol-2-yl)methyl]-1,3,2-dioxaphosphinane-2-oxide;
- 2-[1-Hydroxy-1-(4-[2-{4*H*-3-oxobenzo[1,4]oxazin-2-yl}ethoxy]thiazol-2-yl)methyl]-1,3,2-dioxaphosphinane-2-oxide;
- 20 2-[1-Hydroxy-1-(4-[3,*N*-phthalimidopropoxy]thiazol-2-yl)methyl]-1,3,2-dioxaphosphinane-2-oxide;
- 2-[1-Hydroxy-1-(4-[4,*N*-phthalimidobutoxy]thiazol-2-yl)methyl]-1,3,2-dioxaphosphinane-2-oxide;
- 2[1-(6-[2-{*N*-methyl-*N*-pyrid-2-ylamino}ethoxy]-3-methoxyquinolin-2-yl)-1-(2-oxido-1,3,2-dioxaphospholan-2-yl)methoxy]-1,3,2-dioxaphospholane-2-oxide;

- 2[1-(6-[*N*-(2-{*N*-methyl-*N*-pyrid-2-ylamino}ethyl)-*N*-methylamino]-3-methoxyquinolin-2-yl)-1-(2-oxido-1,3,2-dioxaphospholan-2-yl)methoxy]-1,3,2-dioxaphospholane-2-oxide;
- 5 2[1-(6-[3-{*N*-methyl-*N*-pyrid-2-ylamino}-1-oxoprop-1-yl]-3-methoxyquinolin-2-yl)-1-(2-oxido-1,3,2-dioxaphospholan-2-yl)methoxy]-1,3,2-dioxaphospholane-2-oxide;
- 2[1-(6-[2-{5-methyl-2-phenyloxazol-4-yl}ethoxy]-3-methoxyquinolin-2-yl)-1-(2-oxido-1,3,2-dioxaphospholan-2-yl)methoxy]-1,3,2-dioxaphospholane-2-oxide;
- 10 2[1-(6-[*N*-(2-{5-methyl-2-phenyloxazol-4-yl}ethyl)-*N*-methylamino]-3-methoxyquinolin-2-yl)-1-(2-oxido-1,3,2-dioxaphospholan-2-yl)methoxy]-1,3,2-dioxaphospholane-2-oxide;
- 2[1-(6-[2-{5-methyl-2-phenylthiazol-4-yl}ethoxy]-3-methoxyquinolin-2-yl)-1-(2-oxido-1,3,2-dioxaphospholan-2-yl)methoxy]-1,3,2-dioxaphospholane-2-oxide;
- 15 2[1-(6-[3-{5-methyl-2-phenylthiazol-4-yl}-1-oxoprop-1-yl]-3-methoxyquinolin-2-yl)-1-(2-oxido-1,3,2-dioxaphospholan-2-yl)methoxy]-1,3,2-dioxaphospholane-2-oxide;
- 2[1-(6-[2-{5-methyl-2-pyrid-4-yloxazol-4-yl}ethoxy]-3-methoxyquinolin-2-yl)-1-(2-oxido-1,3,2-dioxaphospholan-2-yl)methoxy]-1,3,2-dioxaphospholane-2-oxide;
- 20 2[1-(6-[2-{5-methyl-2-pyrid-4-ylthiazol-4-yl}ethoxy]-3-methoxyquinolin-2-yl)-1-(2-oxido-1,3,2-dioxaphospholan-2-yl)methoxy]-1,3,2-dioxaphospholane-2-oxide;
- 2[1-(6-[3-{5-methyl-2-pyrid-4-yloxazol-4-yl}-1-oxoprop-1-yl]-3-methoxyquinolin-2-yl)-1-(2-oxido-1,3,2-dioxaphospholan-2-yl)methoxy]-1,3,2-dioxaphospholane-2-oxide;

- 2[1-(6-[*N*-(2-{5-methyl-2-pyrid-4-ylthiazol-4-yl}ethyl)-*N*-methylamino]-3-methoxyquinolin-2-yl)-1-([4*R*]-methyl-2-oxido-1,3,2-dioxaphospholan-2-yl)methoxy]-[4*R*]-methyl-1,3,2-dioxaphospholane-2-oxide;
- 5 2[1-(6-[2-{4-(4-trifluoromethylphenyl)phenoxy}ethoxy]-3-methoxyquinolin-2-yl)-1-([4*R*]-methyl-2-oxido-1,3,2-dioxaphospholan-2-yl)methoxy]-[4*R*]-methyl-1,3,2-dioxaphospholane-2-oxide;
- 2[1-(6-[*N*-(2-{4-(4-trifluoromethylphenyl)phenoxy}ethyl)-*N*-methylamino]-3-methoxyquinolin-2-yl)-1-([4*R*]-methyl-2-oxido-1,3,2-dioxaphospholan-2-yl)methoxy]-[4*R*]-methyl-1,3,2-dioxaphospholane-2-oxide;
- 10 2[1-(6-[3-{4-(4-trifluoromethylphenyl)phenoxy}-1-oxoprop-1-yl]-3-methoxyquinolin-2-yl)-1-([4*R*]-methyl-2-oxido-1,3,2-dioxaphospholan-2-yl)methoxy]-[4*R*]-methyl-1,3,2-dioxaphospholane-2-oxide;
- 2[1-(6-[2-{1-[4-(2-trifluoromethylphenyl)phenylmethyl]-3-hexylureido}ethyl]-3-methoxyquinolin-2-yl)-1-([4*R*]-methyl-2-oxido-1,3,2-dioxaphospholan-2-yl)methoxy]-[4*R*]-methyl-1,3,2-dioxaphospholane-2-oxide;
- 15 2[1-(6-[2-{1-butyl-3-(5-methoxypyrid-2-yl)ureido}ethyl]-3-methoxyquinolin-2-yl)-1-([4*R*]-methyl-2-oxido-1,3,2-dioxaphospholan-2-yl)methoxy]-[4*R*]-methyl-1,3,2-dioxaphospholane-2-oxide;
- 2[1-(6-[3-{4-acetyl-3-hydroxy-2-propylphenoxy}propoxy]-3-methoxyquinolin-2-yl)-1-([4*R*]-methyl-2-oxido-1,3,2-dioxaphospholan-2-yl)methoxy]-[4*R*]-methyl-1,3,2-dioxaphospholane-2-oxide;
- 20 2[1-(6-[2-{4*H*-3-oxobenzo[1,4]oxazin-2-yl}ethoxy]-3-methoxyquinolin-2-yl)-1-([4*R*]-methyl-2-oxido-1,3,2-dioxaphospholan-2-yl)methoxy]-[4*R*]-methyl-1,3,2-dioxaphospholane-2-oxide;

- 2[1-(6-[3,*N*-phthalimidopropoxy]-3-methoxyquinolin-2-yl)-1-([4*R*]-methyl-2-oxido-1,3,2-dioxaphospholan-2-yl)methoxy]-[4*R*]-methyl-1,3,2-dioxaphospholane-2-oxide;
- 5 2[1-(6-[4,*N*-phthalimidobutoxy]-3-methoxyquinolin-2-yl)-1-([4*R*]-methyl-2-oxido-1,3,2-dioxaphospholan-2-yl)methoxy]-[4*R*]-methyl-1,3,2-dioxaphospholane-2-oxide;
- 2[1-(5-[2-{*N*-methyl-*N*-pyrid-2-ylamino}ethoxy]thien-2-yl)-1-([4*S*]-methyl-2-oxido-1,3,2-dioxaphospholan-2-yl)methoxy]-[4*S*]-methyl-1,3,2-dioxaphospholane-2-oxide;
- 10 2[1-(5-[*N*-(2-{*N*-methyl-*N*-pyrid-2-ylamino}ethyl)-*N*-methylamino]thien-2-yl)-1-([4*S*]-methyl-2-oxido-1,3,2-dioxaphospholan-2-yl)methoxy]-[4*S*]-methyl-1,3,2-dioxaphospholane-2-oxide;
- 2[1-(5-[3-{*N*-methyl-*N*-pyrid-2-ylamino}-1-oxoprop-1-yl]thien-2-yl)-1-([4*S*]-methyl-2-oxido-1,3,2-dioxaphospholan-2-yl)methoxy]-[4*S*]-methyl-1,3,2-dioxaphospholane-2-oxide;
- 15 2[1-(5-[2-{5-methyl-2-phenyloxazol-4-yl}ethoxy]thien-2-yl)-1-([4*S*]-methyl-2-oxido-1,3,2-dioxaphospholan-2-yl)methoxy]-[4*S*]-methyl-1,3,2-dioxaphospholane-2-oxide;
- 2[1-(5-[*N*-(2-{5-methyl-2-phenyloxazol-4-yl}ethyl)-*N*-methylamino]thien-2-yl)-1-([4*S*]-methyl-2-oxido-1,3,2-dioxaphospholan-2-yl)methoxy]-[4*S*]-methyl-1,3,2-dioxaphospholane-2-oxide;
- 20 2[1-(5-[2-{5-methyl-2-phenylthiazol-4-yl}ethoxy]thien-2-yl)-1-([4*S*]-methyl-2-oxido-1,3,2-dioxaphospholan-2-yl)methoxy]-[4*S*]-methyl-1,3,2-dioxaphospholane-2-oxide;



- 2[1-(5-[3-{5-methyl-2-phenylthiazol-4-yl}-1-oxoprop-1-yl]thien-2-yl)-1-([4S]-methyl-2-oxido-1,3,2-dioxaphospholan-2-yl)methoxy]-[4S]-methyl-1,3,2-dioxaphospholane-2-oxide;
- 5 2[1-(5-[2-{5-methyl-2-pyrid-4-yloxazol-4-yl}ethoxy]thien-2-yl)-1-([4S]-methyl-2-oxido-1,3,2-dioxaphospholan-2-yl)methoxy]-[4S]-methyl-1,3,2-dioxaphospholane-2-oxide;
- 2[1-(5-[2-{5-methyl-2-pyrid-4-ylthiazol-4-yl}ethoxy]thien-2-yl)-1-([4S]-methyl-2-oxido-1,3,2-dioxaphospholan-2-yl)methoxy]-[4S]-methyl-1,3,2-dioxaphospholane-2-oxide;
- 10 2[1-(5-[3-{5-methyl-2-pyrid-4-yloxazol-4-yl}-1-oxoprop-1-yl]thien-2-yl)-1-([4S]-methyl-2-oxido-1,3,2-dioxaphospholan-2-yl)methoxy]-[4S]-methyl-1,3,2-dioxaphospholane-2-oxide;
- 2[1-(5-[*N*-(2-{5-methyl-2-pyrid-4-ylthiazol-4-yl}ethyl)-*N*-methylamino]thien-2-yl)-1-(4,5-dimethyl-2-oxido-1,3,2-dioxaphospholan-2-yl)methoxy]-4,5-dimethyl-1,3,2-dioxaphospholane-2-oxide;
- 15 2[1-(5-[2-{4-(4-trifluoromethylphenyl)phenoxy}ethoxy]thien-2-yl)-1-(4,5-dimethyl-2-oxido-1,3,2-dioxaphospholan-2-yl)methoxy]-4,5-dimethyl-1,3,2-dioxaphospholane-2-oxide;
- 2[1-(5-[*N*-(2-{4-(4-trifluoromethylphenyl)phenoxy}ethyl)-*N*-methylamino]thien-2-yl)-1-(4,5-dimethyl-2-oxido-1,3,2-dioxaphospholan-2-yl)methoxy]-4,5-dimethyl-1,3,2-dioxaphospholane-2-oxide;
- 20 2[1-(5-[3-{4-(4-trifluoromethylphenyl)phenoxy}-1-oxoprop-1-yl]thien-2-yl)-1-(4,5-dimethyl-2-oxido-1,3,2-dioxaphospholan-2-yl)methoxy]-4,5-dimethyl-1,3,2-dioxaphospholane-2-oxide;

- 2[1-(5-[2-{1-[4-(2-trifluoromethylphenyl)phenylmethyl]-3-hexylureido}ethyl]thien-2-yl)-1-(4,5-dimethyl-2-oxido-1,3,2-dioxaphospholan-2-yl)methoxy]-4,5-dimethyl-1,3,2-dioxaphospholane-2-oxide;
- 5 2[1-(5-[2-{1-butyl-3-(5-methoxypyrid-2-yl)ureido}ethyl]thien-2-yl)-1-(4,5-dimethyl-2-oxido-1,3,2-dioxaphospholan-2-yl)methoxy]-4,5-dimethyl-1,3,2-dioxaphospholane-2-oxide;
- 2[1-(5-[3-{4-acetyl-3-hydroxy-2-propylphenoxy}propoxy]thien-2-yl)-1-(4,5-dimethyl-2-oxido-1,3,2-dioxaphospholan-2-yl)methoxy]-4,5-dimethyl-1,3,2-dioxaphospholane-2-oxide;
- 10 2[1-(5-[2-{4*H*-3-oxobenzo[1,4]oxazin-2-yl}ethoxy]thien-2-yl)-1-(4,5-dimethyl-2-oxido-1,3,2-dioxaphospholan-2-yl)methoxy]-4,5-dimethyl-1,3,2-dioxaphospholane-2-oxide;
- 2[1-(5-[3-*N*-phthalimidopropoxy]thien-2-yl)-1-(4,5-dimethyl-2-oxido-1,3,2-dioxaphospholan-2-yl)methoxy]-4,5-dimethyl-1,3,2-dioxaphospholane-2-oxide;
- 15 2[1-(5-[4-*N*-phthalimidobutoxy]thien-2-yl)-1-(4,5-dimethyl-2-oxido-1,3,2-dioxaphospholan-2-yl)methoxy]-4,5-dimethyl-1,3,2-dioxaphospholane-2-oxide;
- 2[1-(4-[2-{*N*-methyl-*N*-pyrid-2-ylamino}ethoxy]-3-fluorophenyl)-1-(2-oxido-1,3,2-dioxaphosphinan-2-yl)methoxy]-1,3,2-dioxaphosphinane-2-oxide;
- 2[1-(4-[*N*-(2-{*N*-methyl-*N*-pyrid-2-ylamino}ethyl)-*N*-methylaminocarbonyl]-3-fluorophenyl)-1-(2-oxido-1,3,2-dioxaphosphinan-2-yl)methoxy]-1,3,2-dioxaphosphinane-2-oxide;
- 20 2[1-(4-[3-{*N*-methyl-*N*-pyrid-2-ylamino}-1-oxoprop-1-yl]-3-fluorophenyl)-1-(2-oxido-1,3,2-dioxaphosphinan-2-yl)methoxy]-1,3,2-dioxaphosphinane-2-oxide;
- 2[1-(4-[2-{5-methyl-2-phenyloxazol-4-yl}ethoxy]-3-fluorophenyl)-1-(2-oxido-1,3,2-dioxaphosphinan-2-yl)methoxy]-1,3,2-dioxaphosphinane-2-oxide;
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- 1-(4-[*N*-(2-{5-methyl-2-phenyloxazol-4-yl}ethyl)-*N*-methylaminocarbonyl]-3-fluorophenyl)-1,1-bis(2-oxido-1,3,2-dioxaphospholan-2-yl)methane;
- 1-(4-[2-{5-methyl-2-phenylthiazol-4-yl}ethoxy]-3-fluorophenyl)-1,1-bis(2-oxido-1,3,2-dioxaphospholan-2-yl)methane;
- 5 1-(4-[3-{5-methyl-2-phenylthiazol-4-yl}-1-oxoprop-1-yl]-3-fluorophenyl)-1,1-bis(2-oxido-1,3,2-dioxaphospholan-2-yl)methane;
- 1-(4-[2-{5-methyl-2-pyrid-4-yloxazol-4-yl}ethoxy]-3-fluorophenyl)-1,1-bis(2-oxido-1,3,2-dioxaphospholan-2-yl)methane;
- 1-(4-[2-{5-methyl-2-pyrid-4-ylthiazol-4-yl}ethoxy]-3-fluorophenyl)-1,1-bis(4,5-dimethyl-2-oxido-1,3,2-dioxaphospholan-2-yl)methane;
- 10 1-(4-[3-{5-methyl-2-pyrid-4-yloxazol-4-yl}-1-oxoprop-1-yl]-3-fluorophenyl)-1,1-bis(2-oxido-1,3,2-dioxaphosphinan-2-yl)methane;
- 1-(4-[*N*-(2-{5-methyl-2-pyrid-4-ylthiazol-4-yl}ethyl)-*N*-methylaminocarbonyl]-3-fluorophenyl)-1,1-bis(4,5-dimethyl-2-oxido-1,3,2-dioxaphospholan-2-yl)methane;
- 15 1-(4-[2-{4-(4-trifluoromethylphenyl)phenoxy}ethoxy]-3-fluorophenyl)-1,1-bis(2-oxido-1,3,2-dioxaphosphinan-2-yl)methane;
- 1-(4-[*N*-(2-{4-(4-trifluoromethylphenyl)phenoxy}ethyl)-*N*-methylaminocarbonyl]-3-fluorophenyl)-1,1-bis(4,5-dimethyl-2-oxido-1,3,2-dioxaphospholan-2-yl)methane;
- 1-(4-[3-{4-(4-trifluoromethylphenyl)phenoxy}-1-oxoprop-1-yl]-3-fluorophenyl)-1,1-bis(2-oxido-1,3,2-dioxaphosphinan-2-yl)methane;
- 20 1-(4-[2-{1-[4-(2-trifluoromethylphenyl)phenylmethyl]-3-hexylureido}ethyl]-3-fluorophenyl)-1,1-bis(4,5-dimethyl-2-oxido-1,3,2-dioxaphospholan-2-yl)methane;
- 1-(4-[2-{1-butyl-3-(5-methoxypyrid-2-yl)ureido}ethyl]-3-fluorophenyl)-1,1-bis(2-oxido-1,3,2-dioxaphosphinan-2-yl)methane;

- 2-(4-[3-{4-acetyl-3-hydroxy-2-propylphenoxy}propoxy]-3-fluorophenyl)-1,2-bis(2-oxido-1,3,2-dioxaphospholan-2-yl)ethane;
- 2-(4-[2-{4*H*-3-oxobenzo[1,4]oxazin-2-yl}ethoxy]-3-fluorophenyl)-1,2-bis([4*R*]-methyl-2-oxido-1,3,2-dioxaphospholan-2-yl)ethane;
- 5 2-(4-[3,*N*-phthalimidopropoxy]-3-fluorophenyl)-1,2-bis(2-oxido-1,3,2-dioxaphospholan-2-yl)ethane;
- 2-(4-[4,*N*-phthalimidobutoxy]-3-fluorophenyl)-1,2-bis([4*R*]-methyl-2-oxido-1,3,2-dioxaphospholan-2-yl)ethane;
- 2-(3-[3-{*N*-methyl-*N*-pyrid-2-ylamino}propoxy]-4-fluorophenyl)-1,2-bis(2-oxido-1,3,2-dioxaphospholan-2-yl)ethane;
- 10 2-(3-[*N*-(3-{*N*-methyl-*N*-pyrid-2-ylamino}propyl)-*N*-methylamino]-4-fluorophenyl)-1,2-bis([4*R*]-methyl-2-oxido-1,3,2-dioxaphospholan-2-yl)ethane;
- 2-(3-[3-{*N*-methyl-*N*-pyrid-2-ylamino}-1-oxoprop-1-ylamino]-4-fluorophenyl)-1,2-bis(2-oxido-1,3,2-dioxaphospholan-2-yl)ethane;
- 15 2-(3-[3-{5-methyl-2-phenyloxazol-4-yl}propoxy]-4-fluorophenyl)-1,2-bis([4*R*]-methyl-2-oxido-1,3,2-dioxaphospholan-2-yl)ethane;
- 2-(3-[*N*-(2-{5-methyl-2-phenyloxazol-4-yl}ethyl)-*N*-methylaminocarbonyl]-4-methoxyphenyl)-1,1-bis(4,5-dimethyl-2-oxido-1,3,2-dioxaphospholan-2-yl)ethane;
- 20 2-(3-[3-{5-methyl-2-phenylthiazol-4-yl}propoxy]-4-fluorophenyl)-1,1-bis(2-oxido-1,3,2-dioxaphosphinan-2-yl)ethane;
- 2-(3-[3-{5-methyl-2-phenylthiazol-4-yl}-1-oxoprop-1-yl]-4-fluorophenyl)-1,1-bis(4,5-dimethyl-2-oxido-1,3,2-dioxaphospholan-2-yl)ethane;
- 2-(3-[4-{5-methyl-2-pyrid-4-yloxazol-4-yl}butoxy]-4-fluorophenyl)-1,1-bis(2-oxido-1,3,2-dioxaphosphinan-2-yl)ethane;
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- 2-(3-[3-{5-methyl-2-pyrid-4-ylthiazol-4-yl}propoxy]-4-fluorophenyl)-1,1-bis(4,5-dimethyl-2-oxido-1,3,2-dioxaphospholan-2-yl)ethane;
- 2-(3-[3-{5-methyl-2-pyrid-4-yloxazol-4-yl}-1-oxoprop-1-ylthio]-4-fluorophenyl)-1,1-bis(2-oxido-1,3,2-dioxaphosphinan-2-yl)ethane;
- 5 2-(3-[*N*-(3-{5-methyl-2-pyrid-4-ylthiazol-4-yl}propyl)-*N*-methylamino]-4-fluorophenyl)-1,1-bis(4,5-dimethyl-2-oxido-1,3,2-dioxaphospholan-2-yl)ethane;
- 2-(3-[3-{4-(4-trifluoromethylphenyl)phenoxy}propoxy]-4-fluorophenyl)-1,1-bis(2-oxido-1,3,2-dioxaphosphinan-2-yl)ethane;
- 1-[*N*-(3-[*N*-(3-{4-(4-trifluoromethylphenyl)phenoxy}propyl)-*N*-methylamino]-4-fluorophenyl)amino]-1,1-bis(2-oxido-1,3,2-dioxaphospholan-2-yl)methane;
- 10 1-[*N*-(3-[4-{4-(4-trifluoromethylphenyl)phenoxy}-1-oxobut-1-yl]-4-fluorophenyl)amino]-1,1-bis([4*R*]-methyl-2-oxido-1,3,2-dioxaphospholan-2-yl)methane;
- 1-[*N*-(3-[2-{1-[4-(2-trifluoromethylphenyl)phenylmethyl]-3-hexylureido}ethyl]-4-fluorophenyl)amino]-1,1-bis(2-oxido-1,3,2-dioxaphospholan-2-yl)methane;
- 15 1-[*N*-(3-[2-{1-butyl-3-(5-methoxypyrid-2-yl)ureido}ethyl]-4-fluorophenyl)amino]-1,1-bis([4*R*]-methyl-2-oxido-1,3,2-dioxaphospholan-2-yl)methane;
- 1-[*N*-(3-[4-{4-acetyl-3-hydroxy-2-propylphenoxy}butoxy]-4-fluorophenyl)amino]-1,1-bis(2-oxido-1,3,2-dioxaphospholan-2-yl)methane;
- 20 1-[*N*-(3-[3-{4*H*-3-oxobenzo[1,4]oxazin-2-yl}propoxy]-4-fluorophenyl)amino]-1,1-bis([4*R*]-methyl-2-oxido-1,3,2-dioxaphospholan-2-yl)methane;
- 1-[*N*-(3-[3,*N*-phthalimidopropoxy]-4-fluorophenyl)amino]-1,1-bis(2-oxido-1,3,2-dioxaphospholan-2-yl)methane;
- 1-[*N*-(3-[4,*N*-phthalimidobutoxy]-4-fluorophenyl)amino]-1,1-bis([4*R*]-methyl-2-oxido-1,3,2-dioxaphospholan-2-yl)methane;
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- 1-[*N*-(6-[2-{*N*-methyl-*N*-pyrid-2-ylamino}ethoxy]indol-2-yl)amino]-1,1-bis(2-oxido-1,3,2-dioxaphosphinan-2-yl)methane;
- 1-[*N*-(6-[*N*-(2-{*N*-methyl-*N*-pyrid-2-ylamino}ethyl)-*N*-methylamino]indol-2-yl)amino]-1,1-bis(2-oxido-1,3,2-dioxaphosphinan-2-yl)methane;
- 5 1-[*N*-(6-[3-{*N*-methyl-*N*-pyrid-2-ylamino}-1-oxoprop-1-yl]indol-2-yl)amino]-1,1-bis(2-oxido-1,3,2-dioxaphosphinan-2-yl)methane;
- 1-[*N*-(6-[2-{5-methyl-2-phenyloxazol-4-yl}ethoxy] indol-2-yl)amino]-1,1-bis(2-oxido-1,3,2-dioxaphosphinan-2-yl)methane;
- 10 2-[1-(Diethoxyphosphinyloxy)-1-(6-[*N*-(2-{5-methyl-2-phenyloxazol-4-yl}ethyl)-*N*-methylamino] indol-2-yl)methyl]-1,3,2-dioxaphospholane-2-oxide;
- 2-[1-(Diethoxyphosphinyloxy)-1-(6-[2-{5-methyl-2-phenylthiazol-4-yl}ethoxy]indol-2-yl)methyl]-1,3,2-dioxaphospholane-2-oxide;
- 2-[1-(Diethoxyphosphinyloxy)-1-(6-[3-{5-methyl-2-phenylthiazol-4-yl}-1-oxoprop-1-yl]indol-2-yl)methyl]-1,3,2-dioxaphospholane-2-oxide;
- 15 2-[1-(Diethoxyphosphinyloxy)-1-(6-[2-{5-methyl-2-pyrid-4-yloxazol-4-yl}ethoxy]indol-2-yl)methyl]-1,3,2-dioxaphospholane-2-oxide;
- 2-[1-(Diethoxyphosphinyloxy)-1-(6-[2-{5-methyl-2-pyrid-4-ylthiazol-4-yl}ethoxy]indol-2-yl)methyl]-1,3,2-dioxaphosphinane-2-oxide;
- 2-[1-(Diethoxyphosphinyloxy)-1-(6-[3-{5-methyl-2-pyrid-4-yloxazol-4-yl}-1-oxoprop-1-yl]indol-2-yl)methyl]-1,3,2-dioxaphosphinane-2-oxide;
- 20 2-[1-(Diethoxyphosphinyloxy)-1-(6-[*N*-(2-{5-methyl-2-pyrid-4-ylthiazol-4-yl}ethyl)-*N*-methylamino]indol-2-yl)methyl]-1,3,2-dioxaphosphinane-2-oxide;
- 2-[1-(Diethoxyphosphinyloxy)-1-(6-[2-{4-(4-trifluoromethylphenyl)phenoxy}ethoxy]indol-2-yl)methyl]-1,3,2-dioxaphosphinane-2-oxide;

- 2[1-(6-[*N*-(2-{4-(4-trifluoromethylphenyl)phenoxy}ethyl)-*N*-methylamino]indol-2-yl)-1-(diethoxyphosphinyl)methoxy]-4[S]-methyl-1,3,2-dioxaphospholane-2-oxide;
- 2[1-(6-[3-{4-(4-trifluoromethylphenyl)phenoxy}-1-oxoprop-1-yl]indol-2-yl)-1-(diethoxyphosphinyl)methoxy]-4,5-dimethyl-1,3,2-dioxaphospholane-2-oxide;
- 5 2[1-(6-[2-{1-[4-(2-trifluoromethylphenyl)phenylmethyl]-3-hexylureido}ethyl]indol-2-yl)-1-(diethoxyphosphinyl)methoxy]-4[S]-methyl-1,3,2-dioxaphospholane-2-oxide;
- 2[1-(6-[2-{1-[4-(2-trifluoromethylphenyl)phenylmethyl]-3-hexylureido}ethyl]indol-2-yl)-1-(diethoxyphosphinyl)methoxy]-4,5-dimethyl-1,3,2-dioxaphospholane-2-oxide;
- 10 2[1-(6-[3-{4-acetyl-3-hydroxy-2-propylphenoxy}propoxy]indol-2-yl)-1-(diethoxyphosphinyl)methoxy]-4[S]-methyl-1,3,2-dioxaphospholane-2-oxide;
- 2[1-(6-[2-{4*H*-3-oxobenzo[1,4]oxazin-2-yl}ethoxy]indol-2-yl)-1-(diethoxyphosphinyl)methoxy]-4,5-dimethyl-1,3,2-dioxaphospholane-2-oxide;
- 15 2[1-(6-[2-{1-butyl-3-(5-methoxypyrid-2-yl)ureido}ethyl]indol-2-yl)-1-(diethoxyphosphinyl)methoxy]-4[S]-methyl-1,3,2-dioxaphospholane-2-oxide;
- 2[1-(6-[3,*N*-phthalimidopropoxy]indol-2-yl)-1-(diethoxyphosphinyl)methoxy]-4,5-dimethyl-1,3,2-dioxaphospholane-2-oxide;
- 20 2[1-(6-[4,*N*-phthalimidobutoxy]indol-2-yl)-1-(diethoxyphosphinyl)methyl]-4[R]-methyl-1,3,2-dioxaphospholane-2-oxide;
- 2[1-(5-[2-{*N*-methyl-*N*-pyrid-2-ylamino}ethoxy]pyrid-2-yl)-1-(diethoxyphosphinyl)methyl]-4[R]-methyl-1,3,2-dioxaphospholane-2-oxide;
- 2[1-(5-[*N*-(2-{*N*-methyl-*N*-pyrid-2-ylamino}ethyl)-*N*-methylamino]pyrid-2-yl)-1-(diethoxyphosphinyl)methyl]-4[R]-methyl-1,3,2-dioxaphospholane-2-oxide;
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- 2[1-(5-[3-{*N*-methyl-*N*-pyrid-2-ylamino}-1-oxoprop-1-yl]pyrid-2-yl)-1-(diethoxyphosphinyl)methyl]-4[R]-methyl-1,3,2-dioxaphospholane-2-oxide;
- 2[1-(5-[2-{5-methyl-2-phenyloxazol-4-yl}ethoxy]pyrid-2-yl)-1-(diethoxyphosphinyl)methyl]-1,3,2-dioxaphosphinane-2-oxide;
- 5 2[1-(5-[*N*-(2-{5-methyl-2-phenyloxazol-4-yl}ethyl)-*N*-methylamino]pyrid-2-yl)-1-(diethoxyphosphinyl)methyl]-1,3,2-dioxaphosphinane-2-oxide;
- 2[1-(5-[*N*-(2-{5-methyl-2-phenyloxazol-4-yl}ethyl)-*N*-methylamino]pyrid-2-yl)-1-(diethoxyphosphinyl)methyl]-1,3,2-dioxaphosphinane-2-oxide;
- 2[1-(5-[2-{5-methyl-2-phenylthiazol-4-yl}ethoxy]pyrid-2-yl)-1-(diethoxyphosphinyl)methyl]-1,3,2-dioxaphosphinane-2-oxide;
- 10 2[1-(5-[3-{5-methyl-2-phenylthiazol-4-yl}-1-oxoprop-1-yl]pyrid-2-yl)-2-(diethoxyphosphinyl)eth-1-yl]-4,5-dimethyl-1,3,2-dioxaphospholane-2-oxide;
- 2[1-(5-[2-{5-methyl-2-pyrid-4-ylloxazol-4-yl}ethoxy]pyrid-2-yl)-2-(diethoxyphosphinyl)eth-1-yl]-1,3,2-dioxaphosphinane-2-oxide;
- 15 2[1-(5-[2-{5-methyl-2-pyrid-4-ylthiazol-4-yl}ethoxy]pyrid-2-yl)-2-(diethoxyphosphinyl)eth-1-yl]-4,5-dimethyl-1,3,2-dioxaphospholane-2-oxide;
- 2[1-(5-[3-{5-methyl-2-pyrid-4-ylloxazol-4-yl}-1-oxoprop-1-yl]pyrid-2-yl)-2-(diethoxyphosphinyl)eth-1-yl]-1,3,2-dioxaphosphinane-2-oxide;
- 2[1-(5-[*N*-(2-{5-methyl-2-pyrid-4-ylthiazol-4-yl}ethyl)-*N*-methylamino]pyrid-2-yl)-2-(diethoxyphosphinyl)eth-1-yl]-4,5-dimethyl-1,3,2-dioxaphospholane-2-oxide;
- 20 2[1-(5-[2-{4-(4-trifluoromethylphenyl)phenoxy}ethoxy]-pyrid-2-yl)-2-(diethoxyphosphinyl)eth-1-yl]-1,3,2-dioxaphosphinane-2-oxide;
- 2[1-(5-[*N*-(2-{4-(4-trifluoromethylphenyl)phenoxy}ethyl)-*N*-methylamino]pyrid-2-yl)-2-(diethoxyphosphinyl)eth-1-yl]-4,5-dimethyl-1,3,2-dioxaphospholane-2-
- 25 oxide;



- 2[1-(5-[3-{4-(4-trifluoromethylphenyl)phenoxy}-1-oxoprop-1-yl]-pyrid-2-yl)-2-(diethoxyphosphinyl)eth-1-yl]-1,3,2-dioxaphosphinane-2-oxide;
- 2[2-(5-[2-{1-[4-(2-trifluoromethylphenyl)phenylmethyl]-3-hexylureido}ethyl]pyrid-2-yl)-2-(diethoxyphosphinyl)eth-1-yl]-1,3,2-dioxaphospholane-2-oxide;
- 5 2[2-(5-[2-{1-butyl-3-(5-methoxypyrid-2-yl)ureido}ethyl]pyrid-2-yl)-2-(diethoxyphosphinyl)eth-1-yl]-4[R]-methyl-1,3,2-dioxaphospholane-2-oxide;
- 2[2-(5-[3-{4-acetyl-3-hydroxy-2-propylphenoxy}propoxy]pyrid-2-yl)-2-(diethoxyphosphinyl)eth-1-yl]-1,3,2-dioxaphospholane-2-oxide;
- 2[2-(5-[2-{4*H*-3-oxobenzo[1,4]oxazin-2-yl}ethoxy]pyrid-2-yl)-2-(diethoxyphosphinyl)eth-1-yl]-4[R]-methyl-1,3,2-dioxaphospholane-2-oxide;
- 10 2[2-(5-[3,*N*-phthalimidopropoxy]pyrid-2-yl)-2-(diethoxyphosphinyl)eth-1-yl]-1,3,2-dioxaphospholane-2-oxide;
- 2[2-(5-[4,*N*-phthalimidobutoxy]pyrid-2-yl)-2-(diethoxyphosphinyl)eth-1-yl]-4[R]-methyl-1,3,2-dioxaphospholane-2-oxide;
- 15 2[2-(5-[2-{*N*-methyl-*N*-pyrid-2-ylamino}ethoxy]benzothien-2-yl)-2-(diethoxyphosphinyl)eth-1-yl]-1,3,2-dioxaphospholane-2-oxide;
- 2[2-(5-[*N*-(2-{*N*-methyl-*N*-pyrid-2-ylamino}ethyl)-*N*-methyldamino]benzothien-2-yl)-2-(diethoxyphosphinyl)eth-1-yl]-4[R]-methyl-1,3,2-dioxaphospholane-2-oxide;
- 2[2-(5-[3-{*N*-methyl-*N*-pyrid-2-ylamino}-1-oxoprop-1-yl]benzothien-2-yl)-2-(diethoxyphosphinyl)eth-1-yl]-1,3,2-dioxaphosphinane-2-oxide;
- 20 2[2-(5-[2-{5-methyl-2-phenyloxazol-4-yl}ethoxy]benzothien-2-yl)-2-(diethoxyphosphinyl)eth-1-yl]-1,3,2-dioxaphosphinane-2-oxide;
- 2[2-(5-[*N*-(2-{5-methyl-2-phenyloxazol-4-yl}ethyl)-*N*-methyldamino]benzothien-2-yl)-2-(diethoxyphosphinyl)eth-1-yl]-1,3,2-dioxaphosphinane-2-oxide;

- 2[2-(5-[2-{5-methyl-2-phenylthiazol-4-yl}ethoxy]benzothien-2-yl)-2-(diethoxyphosphinyl)eth-1-yl]-1,3,2-dioxaphosphinane-2-oxide;
- 2[2-(5-[3-{5-methyl-2-phenylthiazol-4-yl}-1-oxoprop-1-yl]benzothien-2-yl)-1-(diethoxyphosphinyl)eth-1-yl]-1,3,2-dioxaphospholane-2-oxide;
- 5 2[2-(5-[2-{5-methyl-2-pyrid-4-yloxazol-4-yl}ethoxy]benzothien-2-yl)-1-(diethoxyphosphinyl)eth-1-yl]-1,3,2-dioxaphospholane-2-oxide;
- 2[2-(5-[2-{5-methyl-2-pyrid-4-ylthiazol-4-yl}ethoxy]benzothien-2-yl)-1-(diethoxyphosphinyl)eth-1-yl]-1,3,2-dioxaphospholane-2-oxide;
- 2[2-(5-[3-{5-methyl-2-pyrid-4-yloxazol-4-yl}-1-oxoprop-1-yl]benzothien-2-yl)-1-(diethoxyphosphinyl)eth-1-yl]-1,3,2-dioxaphospholane-2-oxide;
- 10 *N,N,N',N'*-Tetramethyl-1 (5-[*N*-(2-{5-methyl-2-pyrid-4-ylthiazol-4-yl}ethyl)-*N*-methylamino]benzothien-2-yl)-1-hydroxymethylphosphondiamide;
- N,N'*-Diethyl 1-(5-[2-{4-(4-trifluoromethylphenyl)phenoxy}ethoxy]benzothien-2-yl)-1-hydroxymethylphosphondiamide;
- 15 2-[1-hydroxy-1-(5-[*N*-(2-{4-(4-trifluoromethylphenyl)phenoxy}ethyl)-*N*-methylamino]benzothien-2-yl)methyl]-[4*S*,5*S*]-dimethyl-1,3,2-diazaphospholidine-2-oxide;
- 2-[1-hydroxy-1-(5-[3-{4-(4-trifluoromethylphenyl)phenoxy}-1-oxoprop-1-yl]benzothien-2-yl)methyl]-1,3,5,5-tetramethyl-1,3,2-diazaphosphinane-2-oxide;
- 20 2-[1-hydroxy-1-(5-[2-{1-[4-(2-trifluoromethylphenyl)phenylmethyl]-3-hexylureido}ethyl]benzothien-2-yl)methyl]-[4*S*]-ethyl-1,3,2-oxazaphospholidine-2-oxide;
- 2-[1-hydroxy-1-(5-[2-{1-butyl-3-(5-methoxypyrid-2-yl)ureido}ethyl]benzothien-2-yl)methyl]-[4*R*]-methyl-1,3,2-oxazaphosphinane-2-oxide;

- N,N,N',N'*-Tetramethyl-1 (5-[3-{4-acetyl-3-hydroxy-2-propylphenoxy)propoxy]benzothien-2-yl)-1-hydroxymethylphosphondiamide;
- N,N'*-Diethyl 1-(5-[2-{4*H*-3-oxobenzo[1,4]oxazin-2-yl}ethoxy]benzothien-2-yl)-1-hydroxymethylphosphondiamide;
- 5 2-[1-hydroxy-1-(5-[3,*N*-phthalimidopropoxy]benzothien-2-yl)methyl]-[4*S*,5*S*]-dimethyl-1,3,2-diazaphospholidine-2-oxide;
- 2-[1-hydroxy-1-(5-[4,*N*-phthalimidobutoxy]benzothien-2-yl)methyl]-1,3,5,5-tetramethyl-1,3,2-diazaphosphinane-2-oxide;
- 2-[1-hydroxy-1-(4-[2-{*N*-methyl-*N*-pyrid-2-ylamino}ethoxy]thiazol-2-yl)methyl]-[4*S*]-ethyl-1,3,2-oxazaphospholidine-2-oxide;
- 10 2-[1-hydroxy-1-(4-[*N*-(2-{*N*-methyl-*N*-pyrid-2-ylamino}ethyl)-*N*-methylamino]thiazol-2-yl)methyl]-[4*R*]methyl-1,3,2-oxazaphosphinane-2-oxide;
- N,N,N',N'*-Tetramethyl 1-(4-[3-{*N*-methyl-*N*-pyrid-2-ylamino}-1-oxoprop-1-yl]thiazol-2-yl)-1-(bis[*N,N*-dimethylamino]phosphoryloxy)methylphosphondiamide;
- 15 *N,N'*-Diethyl 1-(4-[2-{5-methyl-2-phenyloxazol-4-yl}ethoxy]thiazol-2-yl)-1-(bis[*N*-ethylamino]phosphoryloxy)methylphosphondiamide;
- 2-[1-{([4*S*,5*S*]-dimethyl-2-oxido-1,3,2-diazaphospholidin-2-yl)oxy}-1-(4-[*N*-(2-{5-methyl-2-phenyloxazol-4-yl}ethyl)-*N*-methylamino]thiazol-2-yl)methyl]-[4*S*,5*S*]-dimethyl-1,3,2-diazaphospholidine-2-oxide;
- 20 2-[1-{(1,3,5,5-tetramethyl-2-oxido-1,3,2-diazaphosphinan-2-yl)oxy}-1-(4-[2-{5-methyl-2-phenylthiazol-4-yl}ethoxy]thiazol-2-yl)methyl]-1,3,5,5-tetramethyl-1,3,2-diazaphosphinane-2-oxide;

- 2-[1-{{(4S)-ethyl-2-oxido-1,3,2-oxazaphospholidin-2-yl}oxy}-1-(4-[3-{5-methyl-2-phenylthiazol-4-yl}-1-oxoprop-1-yl]thiazol-2-yl)methyl]-[4S]-ethyl-1,3,2-oxazaphospholidine-2-oxide;
- 2-[1-{{([4R]methyl-1,3,2-oxazaphosphinan-2-yl)oxy}-1-(4-[2-{5-methyl-2-pyrid-4-yloxazol-4-yl}ethoxy]thiazol-2-yl)methyl]-[4R]methyl-1,3,2-oxazaphosphinane-2-oxide;
- N,N,N',N'*-Tetramethyl 1-(4-[2-{5-methyl-2-pyrid-4-ylthiazol-4-yl}ethoxy]thiazol-2-yl)-1-(bis[*N,N*-dimethylamino]phosphoryloxy)methylphosphondiamide;
- N,N'*-Diethyl 1-(4-[3-{5-methyl-2-pyrid-4-yloxazol-4-yl}-1-oxoprop-1-yl]thiazol-2-yl)-1-(bis[*N*-ethylamino]phosphoryloxy)methylphosphondiamide;
- 2-[1-{{([4S,5S]-dimethyl-2-oxido-1,3,2-diazaphospholidin-2-yl)oxy}-1-(4-[*N*-(2-{5-methyl-2-pyrid-4-ylthiazol-4-yl}ethyl)-*N*-methylamino]thiazol-2-yl)methyl]-[4S,5S]-dimethyl-1,3,2-diazaphospholidine-2-oxide;
- 2-[1-{{(1,3,5,5-tetramethyl-2-oxido-1,3,2-diazaphosphinan-2-yl)oxy}-1-(4-[2-{4-(4-trifluoromethylphenyl)phenoxy}ethoxy]thiazol-2-yl)methyl]-1,3,5,5-tetramethyl-1,3,2-diazaphosphinane-2-oxide;
- 2-[1-{{(4S)-ethyl-2-oxido-1,3,2-oxazaphospholidin-2-yl)oxy}-1-(4-[*N*-(2-{4-(4-trifluoromethylphenyl)phenoxy}ethyl)-*N*-methylamino]thiazol-2-yl)methyl]-[4S]-ethyl-1,3,2-oxazaphospholidine-2-oxide;
- 2-[1-{{([4R]methyl-1,3,2-oxazaphosphinan-2-yl)oxy}-1-(4-[3-{4-(4-trifluoromethylphenyl)phenoxy}-1-oxoprop-1-yl]thiazol-2-yl)methyl]-[4R]methyl-1,3,2-oxazaphosphinane-2-oxide;
- 1-(4-[2-{1-[4-(2-trifluoromethylphenyl)phenylmethyl]-3-hexylureido}ethyl]thiazol-2-yl)-1,1-bis(bis[*N,N*-dimethylamino]phosphoryl)methane;

- 1-(4-[2-{1-butyl-3-(5-methoxypyrid-2-yl)ureido}ethyl]thiazol-2-yl)-1,1-bis(bis[*N*-ethylamino]phosphoryl)methane;
- 1-(4-[3-{4-acetyl-3-hydroxy-2-propylphenoxy}propoxy]thiazol-2-yl)-1,1-bis([4*S*,5*S*]-dimethyl-2-oxido-1,3,2-diazaphospholidin-2-yl)methane;
- 5 1-(4-[2-{4*H*-3-oxobenzo[1,4]oxazin-2-yl}ethoxy]thiazol-2-yl)-1,1-bis(1,3,5,5-tetramethyl-2-oxido-1,3,2-diazaphosphinan-2-yl)methane;
- 1-(4-[3,*N*-phthalimidopropoxy]thiazol-2-yl)-1,1-bis ([4*S*]-ethyl-2-oxido-1,3,2-oxazaphospholidin-2-yl)methane;
- 1-(4-[4,*N*-phthalimidobutoxy]thiazol-2-yl)-1,1-bis ([4*R*]methyl-2-oxido-1,3,2-oxazaphosphinan-2-yl)methane;
- 10 1-(6-[2-{*N*-methyl-*N*-pyrid-2-ylamino}ethoxy]-3-methoxyquinolin-2-yl)-1,1-bis(bis[*N,N*-dimethylamino]phosphoryl)methane;
- 1-(6-[*N*-(2-{*N*-methyl-*N*-pyrid-2-ylamino}ethyl)-*N*-methylamino]-3-methoxyquinolin-2-yl)-1,1-bis(bis[*N*-ethylamino]phosphoryl)methane;
- 15 1-(6-[3-{*N*-methyl-*N*-pyrid-2-ylamino}-1-oxoprop-1-yl]-3-methoxyquinolin-2-yl)-1,1-bis([4*S*,5*S*]-dimethyl-2-oxido-1,3,2-diazaphospholidin-2-yl)methane;
- 1-(6-[2-{5-methyl-2-phenyloxazol-4-yl}ethoxy]-3-methoxyquinolin-2-yl)-1,1-bis(1,3,5,5-tetramethyl-2-oxido-1,3,2-diazaphosphinan-2-yl)methane;
- 1-(6-[*N*-(2-{5-methyl-2-phenyloxazol-4-yl}ethyl)-*N*-methylamino]-3-methoxyquinolin-2-yl)-1,1-bis ([4*S*]-ethyl-2-oxido-1,3,2-oxazaphospholidin-2-yl)methane;
- 20 1-(6-[2-{5-methyl-2-phenylthiazol-4-yl}ethoxy]-3-methoxyquinolin-2-yl)-1,1-bis ([4*R*]methyl-2-oxido-1,3,2-oxazaphosphinan-2-yl)methane;
- 1-(6-[3-{5-methyl-2-phenylthiazol-4-yl}-1-oxoprop-1-yl]-3-methoxyquinolin-2-yl)-1,2-bis(bis[*N,N*-dimethylamino]phosphoryl)ethane;
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- 1-(6-[2-{5-methyl-2-pyrid-4-yloxazol-4-yl}ethoxy]-3-methoxyquinolin-2-yl)-1,2-bis(bis[*N*-ethylamino]phosphoryl)ethane;
- 1-(6-[2-{5-methyl-2-pyrid-4-ylthiazol-4-yl}ethoxy]-3-methoxyquinolin-2-yl)-1,2-bis([4*S*,5*S*]-dimethyl-2-oxido-1,3,2-diazaphospholidin-2-yl)ethane;
- 5 1-(6-[3-{5-methyl-2-pyrid-4-yloxazol-4-yl}-1-oxoprop-1-yl]-3-methoxyquinolin-2-yl)-1,2-bis(1,3,5,5-tetramethyl-2-oxido-1,3,2-diazaphosphinan-2-yl)ethane;
- 1-(6-[*N*-(2-{5-methyl-2-pyrid-4-ylthiazol-4-yl}ethyl)-*N*-methylamino]-3-methoxyquinolin-2-yl)-1,2-bis ([4*S*]-ethyl-2-oxido-1,3,2-oxazaphospholidin-2-yl)ethane;
- 10 1-(6-[2-{4-(4-trifluoromethylphenyl)phenoxy}ethoxy]-3-methoxyquinolin-2-yl)-1,2-bis ([4*R*]methyl-2-oxido-1,3,2-oxazaphosphinan-2-yl)ethane;
- 1-(6-[*N*-(2-{4-(4-trifluoromethylphenyl)phenoxy}ethyl)-*N*-methylamino]-3-methoxyquinolin-2-yl)-1,2-bis(bis[*N,N*-dimethylamino]phosphoryl)ethane;
- 1-(6-[3-{4-(4-trifluoromethylphenyl)phenoxy}-1-oxoprop-1-yl]-3-methoxyquinolin-2-yl)-1,2-bis(bis[*N*-ethylamino]phosphoryl)ethane;
- 15 1-(6-[2-{1-[4-(2-trifluoromethylphenyl)phenylmethyl]-3-hexylureido}ethyl]-3-methoxyquinolin-2-yl)-1,2-bis([4*S*,5*S*]-dimethyl-2-oxido-1,3,2-diazaphospholidin-2-yl)ethane;
- 1-(6-[2-{1-butyl-3-(5-methoxypyrid-2-yl)ureido}ethyl]-3-methoxyquinolin-2-yl)-1,2-bis(1,3,5,5-tetramethyl-2-oxido-1,3,2-diazaphosphinan-2-yl)ethane;
- 20 1-(6-[3-{4-acetyl-3-hydroxy-2-propylphenoxy}propoxy]-3-methoxyquinolin-2-yl)-1,2-bis ([4*S*]-ethyl-2-oxido-1,3,2-oxazaphospholidin-2-yl)ethane;
- 1-(6-[3,*N*-phthalimidopropoxy]-3-methoxyquinolin-2-yl)-1,2-bis ([4*R*]methyl-2-oxido-1,3,2-oxazaphosphinan-2-yl)ethane;

- 2-(6-[4,*N*-phthalimidobutoxy]-3-methoxyquinolin-2-yl)-1,1-bis(bis[*N,N*-dimethylamino]phosphoryl)ethane;
- 2-(5-[2-{*N*-methyl-*N*-pyrid-2-ylamino}ethoxy]thien-2-yl)-1,1-bis(bis[*N*-ethylamino]phosphoryl)ethane;
- 5 2-(5-[*N*-(2-{*N*-methyl-*N*-pyrid-2-ylamino}ethyl)-*N*-methylamino]thien-2-yl)-1,1-bis([4*S*,5*S*]-dimethyl-2-oxido-1,3,2-diazaphospholidin-2-yl)ethane;
- 2-(5-[3-{*N*-methyl-*N*-pyrid-2-ylamino}-1-oxoprop-1-yl]thien-2-yl)-1,1-bis(1,3,5,5-tetramethyl-2-oxido-1,3,2-diazaphosphinan-2-yl)ethane;
- 2-(5-[2-{5-methyl-2-phenyloxazol-4-yl}ethoxy]thien-2-yl)-1,1-bis ([4*S*]-ethyl-2-oxido-1,3,2-oxazaphospholidin-2-yl)ethane;
- 10 2-(5-[*N*-(2-{5-methyl-2-phenyloxazol-4-yl}ethyl)-*N*-methylamino]thien-2-yl)-1,1-bis ([4*R*]methyl-2-oxido-1,3,2-oxazaphosphinan-2-yl)ethane;
- 2-(5-[2-{5-methyl-2-phenylthiazol-4-yl}ethoxy]thien-2-yl)-1,1-bis(bis[*N,N*-dimethylamino]phosphoryl)ethane;
- 15 2-(5-[3-{5-methyl-2-phenylthiazol-4-yl}-1-oxoprop-1-yl]thien-2-yl)-1,1-bis(bis[*N*-ethylamino]phosphoryl)ethane;
- 2-(5-[2-{5-methyl-2-pyrid-4-yloxazol-4-yl}ethoxy]thien-2-yl)-1,1-bis([4*S*,5*S*]-dimethyl-2-oxido-1,3,2-diazaphospholidin-2-yl)ethane;
- 2-(5-[2-{5-methyl-2-pyrid-4-ylthiazol-4-yl}ethoxy]thien-2-yl)-1,1-bis(1,3,5,5-tetramethyl-2-oxido-1,3,2-diazaphosphinan-2-yl)ethane;
- 20 2-(5-[3-{5-methyl-2-pyrid-4-yloxazol-4-yl}-1-oxoprop-1-yl]thien-2-yl)-1,1-bis ([4*S*]-ethyl-2-oxido-1,3,2-oxazaphospholidin-2-yl)ethane;
- 2-(5-[*N*-(2-{5-methyl-2-pyrid-4-ylthiazol-4-yl}ethyl)-*N*-methylamino]thien-2-yl)-1,1-bis ([4*R*]methyl-2-oxido-1,3,2-oxazaphosphinan-2-yl)ethane;

- 1-[*N*-(5-[2-{4-(4-trifluoromethylphenyl)phenoxy}ethoxy]thien-2-yl)amino]-1,1-bis(bis[*N,N*-dimethylamino]phosphoryl)methane;
- 1-[*N*-(5-[*N*-(2-{4-(4-trifluoromethylphenyl)phenoxy}ethyl)-*N*-methylamino]thien-2-yl)amino]-1,1-bis(bis[*N*-ethylamino]phosphoryl)methane;
- 5 1-[*N*-(5-[3-{4-(4-trifluoromethylphenyl)phenoxy}-1-oxoprop-1-yl]thien-2-yl)amino]-1,1-bis([4*S*,5*S*]-dimethyl-2-oxido-1,3,2-diazaphospholidin-2-yl)methane;
- 1-[*N*-(5-[2-{1-[4-(2-trifluoromethylphenyl)phenylmethyl]-3-hexylureido}ethyl]thien-2-yl)amino]-1,1-bis(1,3,5,5-tetramethyl-2-oxido-1,3,2-diazaphosphinan-2-yl)methane;
- 10 1-[*N*-(5-[2-{1-butyl-3-(5-methoxypyrid-2-yl)ureido}ethyl]thien-2-yl)amino]-1,1-bis([4*S*]-ethyl-2-oxido-1,3,2-oxazaphospholidin-2-yl)methane;
- 1-[*N*-(5-[3-{4-acetyl-3-hydroxy-2-propylphenoxy}propoxy]thien-2-yl)amino]-1,1-bis([4*R*]-methyl-2-oxido-1,3,2-oxazaphosphinan-2-yl)methane;
- 1-[*N*-(5-[2-{4*H*-3-oxobenzo[1,4]oxazin-2-yl}ethoxy]thien-2-yl)amino]-1,1-bis(bis[*N,N*-dimethylamino]phosphoryl)methane;
- 15 1-[*N*-(5-[3,*N*-phthalimidopropoxy]thien-2-yl)amino]-1,1-bis(bis[*N*-ethylamino]phosphoryl)methane;
- 1-[*N*-(5-[4,*N*-phthalimidobutoxy]thien-2-yl)amino]-1,1-bis([4*S*,5*S*]-dimethyl-2-oxido-1,3,2-diazaphospholidin-2-yl)methane;
- 20 1-[*N*-(4-[2-{*N*-methyl-*N*-pyrid-2-ylamino}ethoxy]-3-fluorophenyl)amino]-1,1-bis(1,3,5,5-tetramethyl-2-oxido-1,3,2-diazaphosphinan-2-yl)methane;
- 1-[*N*-(4-[*N*-(2-{*N*-methyl-*N*-pyrid-2-ylamino}ethyl)-*N*-methylaminocarbonyl]-3-fluorophenyl)amino]-1,1-bis([4*S*]-ethyl-2-oxido-1,3,2-oxazaphospholidin-2-yl)methane;



- 1-[*N*-(4-[3-{*N*-methyl-*N*-pyrid-2-ylamino}-1-oxoprop-1-yl]-3-fluorophenyl)amino]-  
1,1-bis ([4*R*]methyl-2-oxido-1,3,2-oxazaphosphinan-2-yl)methane;
- 2-[1-(Bis[*N*-ethylamino]phosphoryloxy)-1-(4-[2-{5-methyl-2-phenyloxazol-4-  
yl}ethoxy]-3-fluorophenyl)methyl]-[4*S*,5*S*]-dimethyl-1,3,2-diazaphospholidine-2-  
5 oxide;
- 2-[1-(Bis[*N*-ethylamino]phosphoryl)-1-(4-[*N*-(2-{5-methyl-2-phenyloxazol-4-  
yl}ethyl)-*N*-methylaminocarbonyl]-3-fluorophenyl)methoxy]-[4*S*,5*S*]-dimethyl-  
1,3,2-diazaphospholidine-2-oxide;
- 2-[1-(Bis[*N*-ethylamino]phosphoryl)-1-(4-[2-{5-methyl-2-phenylthiazol-4-yl}ethoxy]-  
10 3-fluorophenyl)methyl]-1,3,5,5-tetramethyl-1,3,2-diazaphosphinane-2-oxide;
- 2-[1-(Bis[*N*-ethylamino]phosphoryl)-2-(4-[3-{5-methyl-2-phenylthiazol-4-yl}-1-  
oxoprop-1-yl]-3-fluorophenyl)ethen-1-yl]-[4*S*]-ethyl-1,3,2-oxazaphospholidine-2-  
oxide;
- 2-[1-(Bis[*N*-ethylamino]phosphoryl)-2-(4-[2-{5-methyl-2-pyrid-4-yloxazol-4-  
15 yl}ethoxy]-3-fluorophenyl)eth-1-yl]-[4*R*]methyl-1,3,2-oxazaphosphinane-2-  
oxide;
- 2-[2-(Bis[*N*-ethylamino]phosphoryl)-2-(4-[2-{5-methyl-2-pyrid-4-ylthiazol-4-  
yl}ethoxy]-3-fluorophenyl)eth-1-yl]-1,3,5,5-tetramethyl-1,3,2-diazaphosphinane-  
2-oxide;
- 20 2-[2-(Bis[*N*-ethylamino]phosphoryl)-1-(4-[3-{5-methyl-2-pyrid-4-yloxazol-4-yl}-1-  
oxoprop-1-yl]-3-fluorophenyl)eth-1-yl]-[4*S*]-ethyl-1,3,2-oxazaphospholidine-2-  
oxide;
- 2-[1-(Bis[*N*-ethylamino]phosphoryloxy)-1-(4-[*N*-(2-{5-methyl-2-pyrid-4-ylthiazol-4-  
yl}ethyl)-*N*-methylaminocarbonyl]-3-fluorophenyl)methyl]-[4*S*,5*S*]-dimethyl-  
25 1,3,2-diazaphospholidine-2-oxide;

- 2-[1-(Bis[*N*-ethylamino]phosphoryl)-1-(4-[2-{4-(4-trifluoromethylphenyl)phenoxy}ethoxy]-3-fluorophenyl)methoxy]-[4S,5S]-dimethyl-1,3,2-diazaphospholidine-2-oxide;
- 5 2-[1-(Bis[*N*-ethylamino]phosphoryl)-1-(4-[*N*-(2-{4-(4-trifluoromethylphenyl)phenoxy}ethyl)-*N*-methylaminocarbonyl]-3-fluorophenyl)methyl]-1,3,5,5-tetramethyl-1,3,2-diazaphosphinane-2-oxide;
- 2-[1-(Bis[*N*-ethylamino]phosphoryl)-2-(4-[3-{4-(4-trifluoromethylphenyl)phenoxy}-1-oxoprop-1-yl]-3-fluorophenyl)ethen-1-yl]-[4S]-ethyl-1,3,2-oxazaphospholidine-2-oxide;
- 10 2-[1-(Bis[*N*-ethylamino]phosphoryl)-2-(4-[2-{1-[4-(2-trifluoromethylphenyl)phenylmethyl]-3-hexylureido}ethyl]-3-fluorophenyl)eth-1-yl]-[4R]methyl-1,3,2-oxazaphosphinane-2-oxide;
- 2-[2-(Bis[*N*-ethylamino]phosphoryl)-2-(4-[2-{1-butyl-3-(5-methoxypyrid-2-yl)ureido}ethyl]-3-fluorophenyl)eth-1-yl]-1,3,5,5-tetramethyl-1,3,2-
- 15 diazaphosphinane-2-oxide;
- 2-[2-(Bis[*N*-ethylamino]phosphoryl)-1-(4-[3-{4-acetyl-3-hydroxy-2-propylphenoxy}propoxy]-3-fluorophenyl)eth-1-yl]-[4S]-ethyl-1,3,2-oxazaphospholidine-2-oxide;
- 2-[1-(Diethoxyphosphoryloxy)-1-(4-[2-{4*H*-3-oxobenzo[1,4]oxazin-2-yl}ethoxy]-3-
- 20 fluorophenyl)methyl]-[4S,5S]-dimethyl-1,3,2-diazaphospholidine-2-oxide;
- 2-[1-(Diethoxyphosphoryl)-1-(4-[3,*N*-phthalimidopropoxy]-3-fluorophenyl)methoxy]-[4S,5S]-dimethyl-1,3,2-diazaphospholidine-2-oxide;
- 2-[1-(Diethoxyphosphoryl)-1-(4-[4,*N*-phthalimidobutoxy]-3-fluorophenyl)methyl]-1,3,5,5-tetramethyl-1,3,2-diazaphosphinane-2-oxide;

- 2-[1-(Diethoxyphosphoryl)-2-(3-[3-{*N*-methyl-*N*-pyrid-2-ylamino}propoxy]-4-fluorophenyl)ethen-1-yl]-[4*S*]-ethyl-1,3,2-oxazaphospholidine-2-oxide;
- 2-[1-(Diethoxyphosphoryl)-2-(3-[*N*-(3-{*N*-methyl-*N*-pyrid-2-ylamino}propyl)-*N*-methylamino]-4-fluorophenyl)eth-1-yl]-[4*R*]-methyl-1,3,2-oxazaphosphinane-2-oxide;
- 2-[2-(Diethoxyphosphoryl)-2-(3-[3-{*N*-methyl-*N*-pyrid-2-ylamino}-1-oxoprop-1-ylamino]-4-fluorophenyl)eth-1-yl]-1,3,5,5-tetramethyl-1,3,2-diazaphosphinane-2-oxide;
- 2-[2-(Diethoxyphosphoryl)-1-(3-[3-{5-methyl-2-phenyloxazol-4-yl}propoxy]-4-fluorophenyl)eth-1-yl]-[4*S*]-ethyl-1,3,2-oxazaphospholidine-2-oxide;
- 2-[1-(Diethoxyphosphoryloxy)-1-(3-[*N*-(2-{5-methyl-2-phenyloxazol-4-yl}ethyl)-*N*-methylaminocarbonyl]-4-methoxyphenyl)methyl]-[4*S*,5*S*]-dimethyl-1,3,2-diazaphospholidine-2-oxide;
- 2-[1-(Diethoxyphosphoryl)-1-(3-[3-{5-methyl-2-phenylthiazol-4-yl}propoxy]-4-fluorophenyl)methoxy]-[4*S*,5*S*]-dimethyl-1,3,2-diazaphospholidine-2-oxide;
- 2-[1-(Diethoxyphosphoryl)-1-(3-[3-{5-methyl-2-phenylthiazol-4-yl}-1-oxoprop-1-yl]-4-fluorophenyl)methyl]-1,3,5,5-tetramethyl-1,3,2-diazaphosphinane-2-oxide;
- 2-[1-(Diethoxyphosphoryl)-2-(3-[4-{5-methyl-2-pyrid-4-yloxazol-4-yl}butoxy]-4-fluorophenyl)ethen-1-yl]-[4*S*]-ethyl-1,3,2-oxazaphospholidine-2-oxide;
- 2-[1-(Diethoxyphosphoryl)-2-(3-[3-{5-methyl-2-pyrid-4-ylthiazol-4-yl}propoxy]-4-fluorophenyl)eth-1-yl]-[4*R*]-methyl-1,3,2-oxazaphosphinane-2-oxide;
- 2-[2-(Diethoxyphosphoryl)-2-(3-[3-{5-methyl-2-pyrid-4-yloxazol-4-yl}-1-oxoprop-1-ylthio]-4-fluorophenyl)eth-1-yl]-1,3,5,5-tetramethyl-1,3,2-diazaphosphinane-2-oxide; and

2-[2-(Diethoxyphosphoryl)-1-(3-[*N*-(3-{5-methyl-2-pyrid-4-ylthiazol-4-yl}propyl)-*N*-methylamino]-4-fluorophenyl)eth-1-yl]-[4*S*]-ethyl-1,3,2-oxazaphospholidine-2-oxide.

5           6.       A compound according to Claim 5, wherein the compound is selected from the group consisting of:

Diethyl 1-(diethoxyphosphinyloxy)-1-(4-[2-{*N*-methyl-*N*-pyrid-2-ylamino}ethoxy]-3-fluorophenyl)methylphosphonate;

Diethyl 1-(diethoxyphosphinyloxy)-1-(4-[3,*N*-phthalimidopropoxy]-3-fluorophenyl)methylphosphonate;

Diethyl 1-(diethoxyphosphinyloxy)-1-(4-[2-{5-methyl-2-phenyloxazol-4-yl}ethoxy]-3-fluorophenyl)methylphosphonate;

Diethyl 1-(diethoxyphosphinyloxy)-1-(3-[3-{*N*-methyl-*N*-pyrid-2-ylamino}propoxy]-4-fluorophenyl)methylphosphonate;

Diethyl 1-(diethoxyphosphinyloxy)-1-(3-[4-{*N*-methyl-*N*-pyrid-2-ylamino}butoxy]-4-fluorophenyl)methylphosphonate;

Diethyl 1-(diethoxyphosphinyloxy)-1-(3-[4,*N*-phthalimidobutoxy]-4-fluorophenyl)methylphosphonate;

Diethyl 1-(diethoxyphosphinyloxy)-1-(3-[5,*N*-phthalimidopentoxyl]-4-fluorophenyl)methylphosphonate;

Diethyl 1-(diethoxyphosphinyloxy)-1-(3-[4-{5-methyl-2-pyrid-4-ylloxazol-4-yl}butoxy]-4-fluorophenyl)methylphosphonate;

Diethyl 1-(diethoxyphosphinyloxy)-1-(3-[5-{5-methyl-2-pyrid-4-ylloxazol-4-yl}pentoxyl]-4-fluorophenyl)methylphosphonate;

- 1-(4-[2-{*N*-methyl-*N*-pyrid-2-ylamino}ethoxy]-3-fluorophenyl)-1,1-bis([4*R*,5*S*]-  
dimethyl-2-oxido-1,3,2-dioxaphospholan-2-yl)methane;
- 1-(4-[3,*N*-phthalimidopropoxy]-3-fluorophenyl)-1,1-bis([4*R*,5*S*]-dimethyl-2-oxido-  
1,3,2-dioxaphospholan-2-yl)methane;
- 5 1-(4-[2-{5-methyl-2-phenyloxazol-4-yl}ethoxy]-3-fluorophenyl)-1,1-bis([4*R*,5*S*]-  
dimethyl-2-oxido-1,3,2-dioxaphospholan-2-yl)methane;
- 1-(3-[3-{*N*-methyl-*N*-pyrid-2-ylamino}propoxy]-4-fluorophenyl)-1,1-bis([4*R*,5*S*]-  
dimethyl-2-oxido-1,3,2-dioxaphospholan-2-yl)methane;
- 1-(3-[4-{*N*-methyl-*N*-pyrid-2-ylamino}butoxy]-4-fluorophenyl)-1,1-bis([4*R*,5*S*]-  
10 dimethyl-2-oxido-1,3,2-dioxaphospholan-2-yl)methane;
- 1-(3-[4,*N*-phthalimidobutoxy]-4-fluorophenyl)-1,1-bis([4*R*,5*S*]-dimethyl-2-oxido-  
1,3,2-dioxaphospholan-2-yl)methane;
- 1-(3-[5,*N*-phthalimidopentoxy]-4-fluorophenyl)-1,1-bis([4*R*,5*S*]-dimethyl-2-oxido-  
1,3,2-dioxaphospholan-2-yl)methane;
- 15 1-(3-[4-{5-methyl-2-pyrid-4-yloxazol-4-yl}butoxy]-4-fluorophenyl)-1,1-bis([4*R*,5*S*]-  
dimethyl-2-oxido-1,3,2-dioxaphospholan-2-yl)methane;
- 1-(3-[5-{5-methyl-2-pyrid-4-yloxazol-4-yl}pentoxy]-4-fluorophenyl)-1,1-bis([4*R*,5*S*]-  
dimethyl-2-oxido-1,3,2-dioxaphospholan-2-yl)methane;
- N,N,N',N'*-Tetramethyl 1-(4-[2-{*N*-methyl-*N*-pyrid-2-ylamino}ethoxy]-3-  
20 fluorophenyl)-1-hydroxymethylphosphondiamide;
- N,N,N',N'*-Tetramethyl 1-(4-[3,*N*-phthalimidopropoxy]-3-fluorophenyl)-1-  
hydroxymethylphosphondiamide;
- N,N,N',N'*-Tetramethyl 1-(4-[2-{5-methyl-2-phenyloxazol-4-yl}ethoxy]-3-  
fluorophenyl)-1-hydroxymethylphosphondiamide;

2-[1-hydroxy-1-(4-[2-{*N*-methyl-*N*-pyrid-2-ylamino}ethoxy]-3-fluorophenyl)methyl]-  
[4S]-(1-methylethyl)-1,3,2-oxazaphospholidine-2-oxide;

2-[1-hydroxy-1-(4-[3,*N*-phthalimidopropoxy]-3-fluorophenyl)methyl]-[4S]-(1-  
methylethyl)-1,3,2-oxazaphospholidine-2-oxide;

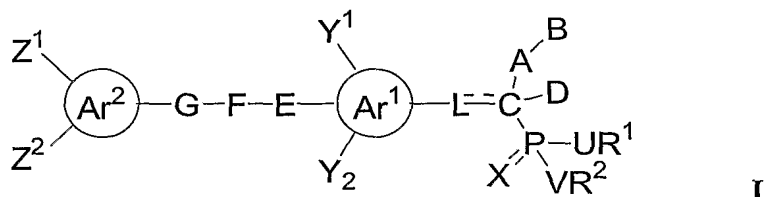
5 2-[1-hydroxy-1-(4-[2-{5-methyl-2-phenyloxazol-4-yl}ethoxy]-3-  
fluorophenyl)methyl]-[4S]-(1-methylethyl)-1,3,2-oxazaphospholidine-2-oxide;

1-[*N*-(4-[2-{*N*-methyl-*N*-pyrid-2-ylamino}ethoxy]-3-fluorophenyl)amino]-1,1-  
bis(bis[*N*-ethylamino]phosphoryl)methane;

1-[*N*-(4-[3,*N*-phthalimidopropoxy]-3-fluorophenyl)amino]-1,1-bis(bis[*N*-  
10 ethylamino]phosphoryl)methane; and

1-[*N*-(4-[2-{5-methyl-2-phenyloxazol-4-yl}ethoxy]-3-fluorophenyl)amino]-1,1-  
bis(bis[*N*-ethylamino]phosphoryl)methane.

7. A pharmaceutical formulation comprising a compound of the formula (I):



wherein

A is a bond, O, CH<sub>2</sub>, CHF, CF<sub>2</sub>, or NR<sub>6</sub>;

B is H, C<sub>1</sub>-C<sub>6</sub> lower alkyl, or P(=X<sup>1</sup>)(UR<sup>3</sup>)(VR<sup>4</sup>);

D is a) H or lower alkyl, wherein the L=C bond is a single bond; or

20 b) OH, OCOR<sup>5</sup>, NH<sub>2</sub>, NR<sup>6</sup>R<sup>6a</sup>, or NHCOR<sup>5</sup>, wherein the L=C bond is a single  
bond, with the proviso that A is CH<sub>2</sub>, CHF, CF<sub>2</sub>;

- L is a)  $\text{NR}^6$ ,  $\text{CR}^7\text{R}^8$ ,  $-\text{OCR}^7\text{R}^8-$ ,  $-\text{NR}^6\text{CR}^7\text{R}^8-$ , or  $-\text{S}(\text{O})_m\text{CR}^7\text{R}^8-$ , wherein the  $\text{L}\equiv\text{C}$  bond is a single bond; or
- b)  $\text{CR}^7$ , wherein the  $\text{L}\equiv\text{C}$  bond is a double bond, with the proviso that D is absent when the  $\text{L}\equiv\text{C}$  bond is a double bond; or
- 5 c) absent, wherein C is covalently bonded by a single bond to  $\text{Ar}^1$ ;
- $\text{Ar}^1$  and  $\text{Ar}^2$  are each independently mono- or bicyclic aromatic rings of 5-12 atoms, including, but not limited to phenyl, pyridyl, pyrimidyl, pyrazinyl, pyridazinyl, thienyl, furanyl, pyrrolyl, imidazolyl, pyrazolyl, oxazolyl, isoxazolyl, thiazolyl, isothiazolyl, 1,3,4-oxadiazolyl, 1,2,4-oxadiazolyl, 1,3,4-thiadiazolyl, 1,2,3-
- 10 triazolyl, 1,3,4-triazolyl, 1,2,4-triazinyl, 1,3,5-triazinyl, benzofuranyl, benzothienyl, indolyl, indazolyl, benzimidazolyl, benzoxazolyl, benzoisoxazolyl, benzothiazolyl, benzoisothiazolyl, quinolyl, isoquinolyl, quinazolinyl, quinoxalinyl, naphthyridyl, or purinyl;
- $\text{Y}^1$ ,  $\text{Y}^2$ , and  $\text{Z}^1$  are each independently a lone electron pair, H,  $\text{C}_1\text{-C}_6$  lower alkyl,  $\text{C}_2\text{-C}_6$  lower alkenyl,  $\text{C}_2\text{-C}_6$  lower alkynyl,  $\text{C}_1\text{-C}_6$  lower alkoxy,  $\text{C}_1\text{-C}_6$  lower alkylamino,  $\text{C}_1\text{-C}_6$  lower dialkylamino,  $\text{C}_2\text{-C}_6$  lower cycloalkyl,  $\text{C}_4\text{-C}_6$  lower cycloalkenyl,  $\text{C}_1\text{-C}_6$  lower thioalkyl,  $\text{C}_1\text{-C}_6$  lower sulfinylalkyl,  $\text{C}_1\text{-C}_6$  lower sulfonylalkyl,  $\text{C}_1\text{-C}_6$  lower acyloxy,  $\text{C}_1\text{-C}_6$  lower acylamino with N substituted with  $\text{R}^6$ ,  $\text{CH}_2\text{OR}^5$ ,  $\text{CH}_2\text{NR}^6\text{R}^{6a}$ ,  $\text{R}_f$ ,  $\text{R}_f\text{O}$ , OH,  $\text{NH}_2$ , CN,  $\text{NO}_2$ , F, Cl, Br, I, or  $\text{N}_3$ ;
- 15 E is a bond,  $\text{S}(\text{O})_m$ ,  $\text{NR}^6$ ,  $\text{C}=\text{O}$ ,  $\text{CO}_2$ ,  $\text{CONR}^6$ , O,  $-\text{OC}=\text{O}$ ,  $\text{NR}^6\text{C}=\text{O}$ ,  $\text{NR}^6\text{CO}_2$ ,  $\text{OC}=\text{ONR}^6$ ,  $\text{OCO}_2$ , or  $\text{NR}^6\text{CONR}^{6a}$ ;
- F is  $(\text{CH}_2)_n$ ,  $(\text{CH}_2)_o\text{O}(\text{CH}_2)_p$ ,  $(\text{CH}_2)_o\text{NR}^6(\text{CH}_2)_p$ ,  $(\text{CH}_2)_o\text{NR}^6\text{CO}(\text{CH}_2)_p$ ,  $(\text{CH}_2)_o\text{CONR}^6(\text{CH}_2)_p$ ,  $(\text{CH}_2)_o(\text{CR}^6=\text{CR}^6)_q(\text{CH}_2)_p$ ,  $(\text{CH}_2)_o-(\text{C}\equiv\text{C})_q-(\text{CH}_2)_p$ ;
- G is a bond, O,  $\text{NR}^6$ , CO,  $\text{CO}_2$ , OCO,  $\text{OCO}_2$ ,  $\text{S}(\text{O})_m$ ,  $\text{CONR}^6$ ,  $\text{NR}^6\text{CO}$ ,  $\text{NR}^6\text{CO}_2$ ,
- 25  $\text{OCONR}^6$ ,  $\text{NR}^6\text{CONR}^{6a}$ , or G can optionally be attached to  $\text{Ar}^2$  at two contiguous

C atoms to form a 5- to 7-membered partially saturated ring, which contains 0, 1, or 2 heteroatoms selected from the group consisting of O, N, and S;

X, X<sup>1</sup> are independently O or S

Z<sup>2</sup> is nothing, H or Ar<sup>1</sup> optionally substituted with Y<sup>1</sup> and Y<sup>2</sup>;

5 R<sup>1</sup>, R<sup>2</sup>, R<sup>3</sup>, and R<sup>4</sup>, are each independently selected from H, C<sub>1</sub>-C<sub>6</sub> lower alkyl, C<sub>3</sub>-C<sub>6</sub> lower alkenyl, C<sub>3</sub>-C<sub>6</sub> lower alkynyl, C<sub>3</sub>-C<sub>6</sub> lower cycloalkyl, C<sub>4</sub>-C<sub>6</sub> lower cycloalkenyl, or independently R<sup>1</sup> and R<sup>2</sup> or R<sup>3</sup> and R<sup>4</sup> can be taken together to form a 5 to 8-membered ring containing 2-7 carbon atoms, the 5 to 8-membered ring optionally substituted with zero to 3 substituents selected from the group C<sub>1</sub>-  
10 C<sub>4</sub> lower alkyl, C<sub>1</sub>-C<sub>4</sub> lower alkoxy, C<sub>1</sub>-C<sub>4</sub> lower alkylamino, C<sub>1</sub>-C<sub>4</sub> lower dialkylamino, amino, hydroxyl, hydroxymethyl, methoxymethyl, phenyl, substituted phenyl, benzyl, substituted benzyl;

U and V are each independently a bond, O or NR<sup>6</sup>;

15 R<sup>5</sup> R<sup>6</sup> and R<sup>6a</sup> are each independently C<sub>1</sub>-C<sub>6</sub> alkyl, C<sub>3</sub>-C<sub>6</sub> cycloalkyl, C<sub>3</sub>-C<sub>6</sub> alkenyl, C<sub>3</sub>-C<sub>6</sub> cycloalkenyl, C<sub>3</sub>-C<sub>6</sub> alkynyl, and H;

R<sup>7</sup> and R<sup>8</sup> are each independently H, C<sub>1</sub>-C<sub>4</sub> lower alkyl, or are taken together to form a saturated C<sub>3</sub>-C<sub>6</sub> carbocyclic ring;

R<sub>f</sub> is C<sub>1</sub>-C<sub>4</sub> straight or branched lower perfluoroalkyl;

all lower alkyl, alkenyl and alkynyl groups including those linked via heteroatoms can  
20 be straight chain or branched;

m is 0, 1, or 2;

n is 0, 1, 2, 3, 4, 5, or 6;

o is 0, 1, 2, 3, 4, 5, or 6;

p is 0, 1, 2, 3, 4, 5, or 6; and

25 q is 0, 1, 2, 3, 4, 5, or 6;



with the provisos that

when A is a bond or O, B is  $P(O)(OR^3)(OR^4)$ , and D is selected from the group H, OH,  $OCOCH_3$ , and  $NH_2$ , and when  $R^1 = R^2$  and  $R^3 = R^4$ , and both are selected from the group H or unsubstituted  $C_1$ - $C_4$  lower alkyl, and E and G are bonds, and F is  
 5  $(CH_2)_n$  where n is 0, and both  $Ar^1$  and  $Ar^2$  are phenyl, then at least one of  $Y^1$ ,  $Y^2$ ,  $Z^1$ , or  $Z^2$  must not be H; and

when A is a bond or  $CH_2$ , and B is  $P(O)(OR^3)(OR^4)$ , and either D is H or  $C_1$ - $C_4$  lower alkyl where L is  $CH_2$ , or D is absent, with  $L=C$  taken together represent an ethenylidene group, and  $Ar^1$  is phenyl, and E is a bond or O, and  $R^1 = R^2$  and  $R^3 = R^4$ ,  
 10 and both are drawn from the group H or  $C_1$ - $C_6$  unsubstituted lower alkyl, then one of  $Y^1$  and  $Y^2$  must be other than H or unsubstituted  $C_1$ - $C_4$  lower alkyl or unsubstituted  $C_1$ - $C_4$  lower alkoxy; and

when A is O, and B is H or  $P(O)(OR^3)(OR^4)$ , and  $R^1$ ,  $R^2$ ,  $R^3$ , and  $R^4$  are all selected from the group H or  $C_1$ - $C_6$  unsubstituted lower alkyl, and D is H, and L is a  
 15 bond, and  $Ar^1$  is phenyl, and E is other than a bond or O, then one of  $Y^1$  or  $Y^2$  must be other than H, or  $C_1$ - $C_4$  unsubstituted lower alkyl or  $C_1$ - $C_4$  unsubstituted lower alkoxy;

and a pharmaceutically acceptable carrier, excipient, solvent, adjuvant or diluent.

20 8. The pharmaceutical composition according to Claim 7, wherein in the compound of Formula I,

A is selected from a bond, O, and  $CH_2$ ;

B is  $P(=O)(UR^3)(VR^4)$ ;

D is H; and

25 the  $L=C$  bond is a single bond.

9. The pharmaceutical formulation according to Claim 8, wherein Ar<sup>1</sup> in Formula I is phenyl.

5 10. The pharmaceutical formulation according to Claim 9, wherein U and V in Formula I are each O.

11. The pharmaceutical formulation according to Claim 7, wherein the compound of Formula I is selected from the group consisting of:

10 Diethyl 1-(diethoxyphosphinyloxy)-1-(4-[2-{*N*-methyl-*N*-pyrid-2-ylamino}ethoxy]-3-fluorophenyl)methylphosphonate;

Diethyl 1-(diethoxyphosphinyloxy)-1-(4-[*N*-(2-{*N*-methyl-*N*-pyrid-2-ylamino}ethyl)-*N*-methylaminocarbonyl]-3-fluorophenyl)methylphosphonate;

15 Diethyl 1-(diethoxyphosphinyloxy)-1-(4-[3-{*N*-methyl-*N*-pyrid-2-ylamino}-1-oxoprop-1-yl]-3-fluorophenyl)methylphosphonate;

Diethyl 1-(diethoxyphosphinyloxy)-1-(4-[2-{5-methyl-2-phenyloxazol-4-yl}ethoxy]-3-fluorophenyl)methylphosphonate;

Diethyl 1-(diethoxyphosphinyloxy)-1-(4-[*N*-(2-{5-methyl-2-phenyloxazol-4-yl}ethyl)-*N*-methylaminocarbonyl]-3-fluorophenyl)methylphosphonate;

20 Diethyl 1-(diethoxyphosphinyloxy)-1-(4-[2-{5-methyl-2-phenylthiazol-4-yl}ethoxy]-3-fluorophenyl)methylphosphonate;

Diethyl 1-(diethoxyphosphinyloxy)-1-(4-[3-{5-methyl-2-phenylthiazol-4-yl}-1-oxoprop-1-yl]-3-fluorophenyl)methylphosphonate;

25 Diethyl 1-(diethoxyphosphinyloxy)-1-(4-[2-{5-methyl-2-pyrid-4-yloxazol-4-yl}ethoxy]-3-fluorophenyl)methylphosphonate;

- Diethyl 1-(diethoxyphosphinyloxy)-1-(4-[2-{5-methyl-2-pyrid-4-ylthiazol-4-yl}ethoxy]-3-fluorophenyl)methylphosphonate;
- Diethyl 1-(diethoxyphosphinyloxy)-1-(4-[3-{5-methyl-2-pyrid-4-yloxazol-4-yl}-1-oxoprop-1-yl]-3-fluorophenyl)methylphosphonate;
- 5 Diethyl 1-(hydroxy)-1-(4-[*N*-(2-{5-methyl-2-pyrid-4-ylthiazol-4-yl}ethyl)-*N*-methylaminocarbonyl]-3-fluorophenyl)methylphosphonate;
- Diethyl 1-(hydroxy)-1-(4-[2-{4-(4-trifluoromethylphenyl)phenoxy}ethoxy]-3-fluorophenyl)methylphosphonate;
- Diethyl 1-(hydroxy)-1-(4-[*N*-(2-{4-(4-trifluoromethylphenyl)phenoxy}ethyl)-*N*-methylaminocarbonyl]-3-fluorophenyl)methylphosphonate;
- 10 Diethyl 1-(hydroxy)-1-(4-[3-{4-(4-trifluoromethylphenyl)phenoxy}-1-oxoprop-1-yl]-3-fluorophenyl)methylphosphonate;
- Diethyl 1-(hydroxy)-1-(4-[2-{1-[4-(2-trifluoromethylphenyl)phenylmethyl]-3-hexylureido}ethyl]-3-fluorophenyl)methylphosphonate;
- 15 Diethyl 1-(hydroxy)-1-(4-[2-{1-butyl-3-(5-methoxypyrid-2-yl)ureido}ethyl]-3-fluorophenyl)methylphosphonate;
- Diethyl 1-(hydroxy)-1-(4-[3-{4-acetyl-3-hydroxy-2-propylphenoxy}propoxy]-3-fluorophenyl)methylphosphonate;
- Diethyl 1-(hydroxy)-1-(4-[2-{4*H*-3-oxobenzo[1,4]oxazin-2-yl}ethoxy]-3-fluorophenyl)methylphosphonate;
- 20 Diethyl 1-(hydroxy)-1-(4-[3,*N*-phthalimidopropoxy]-3-fluorophenyl)methylphosphonate;
- Diethyl 1-(hydroxy)-1-(4-[4,*N*-phthalimidobutoxy]-3-fluorophenyl)methylphosphonate;

- Tetraethyl 1-(3-[3-{*N*-methyl-*N*-pyrid-2-ylamino}propoxy]-4-fluorophenyl  
)methylidenebisphosphonate;
- Tetraethyl 1-(3-[*N*-(3-{*N*-methyl-*N*-pyrid-2-ylamino}propyl)-*N*-methylanino]-4-  
fluorophenyl)methylidenebisphosphonate;
- 5 Tetraethyl 1-(3-[3-{*N*-methyl-*N*-pyrid-2-ylamino}-1-oxoprop-1-ylamino]-4-  
fluorophenyl)methylidenebisphosphonate;
- Tetraethyl 1-(3-[3-{5-methyl-2-phenyloxazol-4-yl}propoxy]-4-  
fluorophenyl)methylidenebisphosphonate;
- Tetraethyl 1-(3-[*N*-(2-{5-methyl-2-phenyloxazol-4-yl}ethyl)-*N*-  
10 methylaminocarbonyl]-4-methoxyphenyl)methylidenebisphosphonate;
- Tetraethyl 1-(3-[3-{5-methyl-2-phenylthiazol-4-yl}propoxy]-4-  
fluorophenyl)methylidenebisphosphonate;
- Tetraethyl 1-(3-[3-{5-methyl-2-phenylthiazol-4-yl}-1-oxoprop-1-yl]-4-  
fluorophenyl)methylidenebisphosphonate;
- 15 Tetraethyl 1-(3-[4-{5-methyl-2-pyrid-4-yloxazol-4-yl}butoxy]-4-  
fluorophenyl)methylidenebisphosphonate;
- Tetraethyl 1-(3-[3-{5-methyl-2-pyrid-4-ylthiazol-4-yl}propoxy]-4-  
fluorophenyl)methylidenebisphosphonate;
- Tetraethyl 1-(3-[3-{5-methyl-2-pyrid-4-yloxazol-4-yl}-1-oxoprop-1-ylthio]-4-  
20 fluorophenyl)methylidenebisphosphonate;
- Tetraethyl 2-(3-[*N*-(3-{5-methyl-2-pyrid-4-ylthiazol-4-yl}propyl)-*N*-methylanino]-4-  
fluorophenyl)vinylidene-1,1-bisphosphonate;
- Tetraethyl 2-(3-[3-{4-(4-trifluoromethylphenyl)phenoxy}propoxy]-4-  
fluorophenyl)vinylidene-1,1-bisphosphonate;

- Tetraethyl 2-(3-[*N*-(3-{4-(4-trifluoromethylphenyl)phenoxy}propyl)-*N*-methylamino]-4-fluorophenyl)vinylidene-1,1-bisphosphonate;
- Tetraethyl 2-(3-[4-{4-(4-trifluoromethylphenyl)phenoxy}-1-oxobut-1-yl]-4-fluorophenyl)vinylidene-1,1-bisphosphonate;
- 5 Tetraethyl 2-(3-[2-{1-[4-(2-trifluoromethylphenyl)phenylmethyl]-3-hexylureido}ethyl]-4-fluorophenyl)vinylidene-1,1-bisphosphonate;
- Tetraethyl 2-(3-[2-{1-butyl-3-(5-methoxypyrid-2-yl)ureido}ethyl]-4-fluorophenyl)vinylidene-1,1-bisphosphonate;
- Tetraethyl 2-(3-[4-{4-acetyl-3-hydroxy-2-propylphenoxy}butoxy]-4-fluorophenyl)vinylidene-1,1-bisphosphonate;
- 10 Tetraethyl 2-(3-[3-{4*H*-3-oxobenzo[1,4]oxazin-2-yl}propoxy]-4-fluorophenyl)vinylidene-1,1-bisphosphonate;
- Tetraethyl 2-(3-[3-*N*-phthalimidopropoxy]-4-fluorophenyl)vinylidene-1,1-bisphosphonate;
- 15 Tetraethyl 2-(3-[4-*N*-phthalimidobutoxy]-4-fluorophenyl)vinylidene-1,1-bisphosphonate;
- Tetraethyl 1-(6-[2-{*N*-methyl-*N*-pyrid-2-ylamino}ethoxy]indol-2-yl)ethylidene-1,2-bisphosphonate;
- Tetraethyl 1-(6-[*N*-(2-{*N*-methyl-*N*-pyrid-2-ylamino}ethyl)-*N*-methylamino]indol-2-yl)ethylidene-1,2-bisphosphonate;
- 20 Tetraethyl 1-(6-[3-{*N*-methyl-*N*-pyrid-2-ylamino}-1-oxoprop-1-yl]indol-2-yl)ethylidene-1,2-bisphosphonate;
- Tetraethyl 1-(6-[2-{5-methyl-2-phenyloxazol-4-yl}ethoxy]indol-2-yl)ethylidene-1,2-bisphosphonate;

- Tetraethyl 1-(6-[*N*-(2-{5-methyl-2-phenyloxazol-4-yl}ethyl)-*N*-methylamino] indol-2-yl)ethylidene-1,2-bisphosphonate;
- Tetraethyl 1-(6-[2-{5-methyl-2-phenylthiazol-4-yl}ethoxy]indol-2-yl)ethylidene-1,2-bisphosphonate;
- 5 Tetraethyl 1-(6-[3-{5-methyl-2-phenylthiazol-4-yl}-1-oxoprop-1-yl]indol-2-yl)ethylidene-1,2-bisphosphonate;
- Tetraethyl 1-(6-[2-{5-methyl-2-pyrid-4-yloxazol-4-yl}ethoxy]indol-2-yl)ethylidene-1,2-bisphosphonate;
- Tetraethyl 1-(6-[2-{5-methyl-2-pyrid-4-ylthiazol-4-yl}ethoxy]indol-2-yl)ethylidene-1,2-bisphosphonate;
- 10 Tetraethyl 1-(6-[3-{5-methyl-2-pyrid-4-yloxazol-4-yl}-1-oxoprop-1-yl]indol-2-yl)ethylidene-1,2-bisphosphonate;
- Tetraethyl 2-(6-[*N*-(2-{5-methyl-2-pyrid-4-ylthiazol-4-yl}ethyl)-*N*-methylamino]indol-2-yl)ethylidene-1,1-bisphosphonate;
- 15 Tetraethyl 2-(6-[2-{4-(4-trifluoromethylphenyl)phenoxy}ethoxy] indol-2-yl)ethylidene-1,1-bisphosphonate;
- Tetraethyl 2-(6-[*N*-(2-{4-(4-trifluoromethylphenyl)phenoxy}ethyl)-*N*-methylamino]indol-2-yl)ethylidene-1,1-bisphosphonate;
- Tetraethyl 2-(6-[2-{1-[4-(2-trifluoromethylphenyl)phenylmethyl]-3-hexylureido}ethyl]indol-2-yl)ethylidene-1,1-bisphosphonate;
- 20 Tetraethyl 2-(6-[2-{1-butyl-3-(5-methoxypyrid-2-yl)ureido}ethyl]indol-2-yl)ethylidene-1,1-bisphosphonate;
- Tetraethyl 2-(6-[3-{4-(4-trifluoromethylphenyl)phenoxy}-1-oxoprop-1-yl]indol-2-yl)ethylidene-1,1-bisphosphonate;

- Tetraethyl 2-(6-[3-{4-acetyl-3-hydroxy-2-propylphenoxy}propoxy]indol-2-yl)ethylidene-1,1-bisphosphonate;
- Tetraethyl 2-(6-[2-{4*H*-3-oxobenzo[1,4]oxazin-2-yl}ethoxy]indol-2-yl)ethylidene-1,1-bisphosphonate;
- 5 Tetraethyl 2-(6-[3-*N*-phthalimidopropoxy]indol-2-yl)ethylidene-1,1-bisphosphonate;
- Tetraethyl 2-(6-[4-*N*-phthalimidobutoxy]indol-2-yl)ethylidene-1,1-bisphosphonate;
- Tetraethyl *N*-(5-[2-{*N*-methyl-*N*-pyrid-2-ylamino}ethoxy]pyrid-2-yl)aminomethylidenebisphosphonate;
- Tetraethyl *N*-(5-[*N*-(2-{*N*-methyl-*N*-pyrid-2-ylamino}ethyl)-*N*-methylamino]pyrid-2-yl)aminomethylidenebisphosphonate;
- 10 Tetraethyl *N*-(5-[3-{*N*-methyl-*N*-pyrid-2-ylamino}-1-oxoprop-1-yl]pyrid-2-yl)aminomethylidenebisphosphonate;
- Tetraethyl *N*-(5-[2-{5-methyl-2-phenyloxazol-4-yl}ethoxy]pyrid-2-yl)aminomethylidenebisphosphonate;
- 15 Tetraethyl *N*-(5-[*N*-(2-{5-methyl-2-phenyloxazol-4-yl}ethyl)-*N*-methylamino]pyrid-2-yl)aminomethylidenebisphosphonate;
- Tetraethyl *N*-(5-[2-{5-methyl-2-phenylthiazol-4-yl}ethoxy]pyrid-2-yl)aminomethylidenebisphosphonate;
- Tetraethyl *N*-(5-[3-{5-methyl-2-pyrid-4-yloxazol-4-yl}-1-oxoprop-1-yl]pyrid-2-yl)aminomethylidenebisphosphonate;
- 20 Tetraethyl *N*-(5-[*N*-(2-{5-methyl-2-pyrid-4-ylthiazol-4-yl}ethyl)-*N*-methylamino]pyrid-2-yl)aminomethylidenebisphosphonate;
- Tetraethyl *N*-(5-[2-{5-methyl-2-pyrid-4-yloxazol-4-yl}ethoxy]pyrid-2-yl)aminomethylidenebisphosphonate;

- Tetraethyl *N*-(5-[2-{5-methyl-2-pyrid-4-ylthiazol-4-yl}ethoxy]pyrid-2-yl)aminomethylidenebisphosphonate;
- 2-[1-Hydroxy-1-(5-[*N*-(2-{5-methyl-2-pyrid-4-ylthiazol-4-yl}ethyl)-*N*-methylamino]pyrid-2-yl)methyl]-1,3,2-dioxaphospholane-2-oxide;
- 5 2-[1-Hydroxy-1-(5-[2-{4-(4-trifluoromethylphenyl)phenoxy}ethoxy]-pyrid-2-yl)methyl]-1,3,2-dioxaphospholane-2-oxide;
- 2-[1-Hydroxy-1-(5-[*N*-(2-{4-(4-trifluoromethylphenyl)phenoxy}ethyl)-*N*-methylamino]pyrid-2-yl)methyl]-1,3,2-dioxaphospholane-2-oxide;
- 2-[1-Hydroxy-1-(5-[3-{4-(4-trifluoromethylphenyl)phenoxy}-1-oxoprop-1-yl]-pyrid-10 2-yl)methyl]-1,3,2-dioxaphospholane-2-oxide;
- 2-[1-Hydroxy-1-(5-[2-{1-[4-(2-trifluoromethylphenyl)phenylmethyl]-3-hexylureido}ethyl]pyrid-2-yl)methyl]-1,3,2-dioxaphospholane-2-oxide;
- 2-[1-Hydroxy-1-(5-[2-{1-butyl-3-(5-methoxypyrid-2-yl)ureido}ethyl]pyrid-2-ylmethyl)-1,3,2-dioxaphospholane-2-oxide;
- 15 2-[1-Hydroxy-15-[3-{4-acetyl-3-hydroxy-2-propylphenoxy}propoxy]pyrid-2-ylmethyl]-1,3,2-dioxaphospholane-2-oxide;
- 2-[1-Hydroxy-1-(5-[2-{4*H*-3-oxobenzo[1,4]oxazin-2-yl}ethoxy]pyrid-2-yl)methyl]-1,3,2-dioxaphospholane-2-oxide;
- 2-[1-Hydroxy-1-(5-[3,*N*-phthalimidopropoxy]pyrid-2-yl)methyl]-1,3,2-dioxaphospholane-2-oxide;
- 20 2-[1-Hydroxy-1-(5-[4,*N*-phthalimidobutoxy]pyrid-2-yl)methyl]-1,3,2-dioxaphospholane-2-oxide;
- 2-[1-Hydroxy-1-(5-[2-{*N*-methyl-*N*-pyrid-2-ylamino}ethoxy]benzothien-2-yl)methyl]- [4*R*]-methyl-1,3,2-dioxaphospholane-2-oxide;



- 2-[1-Hydroxy-1-(5-[*N*-(2-{*N*-methyl-*N*-pyrid-2-ylamino}ethyl)-*N*-methylamino]benzothien-2-yl)methyl]- [4R]-methyl-1,3,2-dioxaphospholane-2-oxide;
- 2-[1-Hydroxy-1-(5-[3-{*N*-methyl-*N*-pyrid-2-ylamino}-1-oxoprop-1-yl]benzothien-2-yl)methyl]- [4R]-methyl-1,3,2-dioxaphospholane-2-oxide;
- 5 2-[1-Hydroxy-1-(5-[2-{5-methyl-2-phenyloxazol-4-yl}ethoxy]benzothien-2-yl)methyl]- [4R]-methyl-1,3,2-dioxaphospholane-2-oxide;
- 2-[1-Hydroxy-1-(5-[2-{5-methyl-2-phenyloxazol-4-yl}ethyl)-*N*-methylamino]benzothien-2-yl)methyl]- [4R]-methyl-1,3,2-dioxaphospholane-2-oxide;
- 10 2-[1-Hydroxy-1-(5-[2-{5-methyl-2-phenylthiazol-4-yl}ethoxy]benzothien-2-yl)methyl]- [4R]-methyl-1,3,2-dioxaphospholane-2-oxide;
- 2-[1-Hydroxy-1-(5-[3-{5-methyl-2-phenylthiazol-4-yl}-1-oxoprop-1-yl]benzothien-2-yl)methyl]- [4R]-methyl-1,3,2-dioxaphospholane-2-oxide;
- 15 2-[1-Hydroxy-1-(5-[2-{5-methyl-2-pyrid-4-ylloxazol-4-yl}ethoxy]benzothien-2-yl)methyl]- [4R]-methyl-1,3,2-dioxaphospholane-2-oxide;
- 2-[1-Hydroxy-1-(5-[2-{5-methyl-2-pyrid-4-ylthiazol-4-yl}ethoxy]benzothien-2-yl)methyl]- [4R]-methyl-1,3,2-dioxaphospholane-2-oxide;
- 2-[1-Hydroxy-1-(5-[3-{5-methyl-2-pyrid-4-ylloxazol-4-yl}-1-oxoprop-1-yl]benzothien-2-yl)methyl]- [4R]-methyl-1,3,2-dioxaphospholane-2-oxide;
- 20 2-[1-Hydroxy-1-(5-[*N*-(2-{5-methyl-2-pyrid-4-ylthiazol-4-yl}ethyl)-*N*-methylamino]benzothien-2-yl)methyl]- [4S]-methyl-1,3,2-dioxaphospholane-2-oxide;
- 2-[1-Hydroxy-1-(5-[2-{4-(4-trifluoromethylphenyl)phenoxy}ethoxy]benzothien-2-yl)methyl]- [4S]-methyl-1,3,2-dioxaphospholane-2-oxide;
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- 2-[1-Hydroxy-1-(5-[*N*-(2-{4-(4-trifluoromethylphenyl)phenoxy}ethyl)-*N*-methylamino]benzothien-2-yl)methyl]- [4*S*]-methyl-1,3,2-dioxaphospholane-2-oxide;
- 2-[1-Hydroxy-1-(5-[3-{4-(4-trifluoromethylphenyl)phenoxy}-1-oxoprop-1-yl]benzothien-2-yl)methyl]- [4*S*]-methyl-1,3,2-dioxaphospholane-2-oxide;
- 5 2-[1-Hydroxy-1-(5-[2-{1-[4-(2-trifluoromethylphenyl)phenylmethyl]-3-hexylureido}ethyl]benzothien-2-yl)methyl]- [4*S*]-methyl-1,3,2-dioxaphospholane-2-oxide;
- 2-[1-Hydroxy-1-(5-[2-{1-butyl-3-(5-methoxypyrid-2-yl)ureido}ethyl]benzothien-2-yl)methyl]- [4*S*]-methyl-1,3,2-dioxaphospholane-2-oxide;
- 10 2-[1-Hydroxy-1-(5-[3-{4-acetyl-3-hydroxy-2-propylphenoxy}propoxy]benzothien-2-yl)methyl]- [4*S*]-methyl-1,3,2-dioxaphospholane-2-oxide;
- 2-[1-Hydroxy-1-(5-[2-{4*H*-3-oxobenzo[1,4]oxazin-2-yl}ethoxy]benzothien-2-yl)methyl]- [4*S*]-methyl-1,3,2-dioxaphospholane-2-oxide;
- 15 2-[1-Hydroxy-1-(5-[3,*N*-phthalimidopropoxy]benzothien-2-yl)methyl]- [4*S*]-methyl-1,3,2-dioxaphospholane-2-oxide;
- 2-[1-Hydroxy-1-(5-[4,*N*-phthalimidobutoxy]benzothien-2-yl)methyl]- [4*S*]-methyl-1,3,2-dioxaphospholane-2-oxide;
- 2-[1-Hydroxy-1-(4-[2-{*N*-methyl-*N*-pyrid-2-ylamino}ethoxy]thiazol-2-yl)methyl]-
- 20 4,5-dimethyl-1,3,2-dioxaphospholane-2-oxide;
- 2-[1-Hydroxy-1-(4-[*N*-(2-{*N*-methyl-*N*-pyrid-2-ylamino}ethyl)-*N*-methylamino]thiazol-2-yl)methyl]-4,5-dimethyl-1,3,2-dioxaphospholane-2-oxide;
- 2-[1-Hydroxy-1-(4-[3-{*N*-methyl-*N*-pyrid-2-ylamino}-1-oxoprop-1-yl]thiazol-2-yl)methyl]-4,5-dimethyl-1,3,2-dioxaphospholane-2-oxide;

- 2-[1-Hydroxy-1-(4-[2-{5-methyl-2-phenyloxazol-4-yl}ethoxy]thiazol-2-yl)methyl]-  
4,5-dimethyl-1,3,2-dioxaphospholane-2-oxide;
- 2-[1-Hydroxy-1-(4-[*N*-(2-{5-methyl-2-phenyloxazol-4-yl}ethyl)-*N*-  
methylamino]thiazol-2-yl)methyl]-4,5-dimethyl-1,3,2-dioxaphospholane-2-oxide;
- 5 2-[1-Hydroxy-1-(4-[2-{5-methyl-2-phenylthiazol-4-yl}ethoxy]thiazol-2-yl)methyl]-  
4,5-dimethyl-1,3,2-dioxaphospholane-2-oxide;
- 2-[1-Hydroxy-1-(4-[3-{5-methyl-2-phenylthiazol-4-yl}-1-oxoprop-1-yl]thiazol-2-  
yl)methyl]-4,5-dimethyl-1,3,2-dioxaphospholane-2-oxide;
- 2-[1-Hydroxy-1-(4-[2-{5-methyl-2-pyrid-4-ylloxazol-4-yl}ethoxy]thiazol-2-  
10 yl)methyl]-4,5-dimethyl-1,3,2-dioxaphospholane-2-oxide;
- 2-[1-Hydroxy-1-(4-[2-{5-methyl-2-pyrid-4-ylthiazol-4-yl}ethoxy]thiazol-2-  
yl)methyl]-4,5-dimethyl-1,3,2-dioxaphospholane-2-oxide;
- 2-[1-Hydroxy-1-(4-[3-{5-methyl-2-pyrid-4-ylloxazol-4-yl}-1-oxoprop-1-yl]thiazol-2-  
yl)methyl]-4,5-dimethyl-1,3,2-dioxaphospholane-2-oxide;
- 15 2-[1-Hydroxy-1-(4-[*N*-(2-{5-methyl-2-pyrid-4-ylthiazol-4-yl}ethyl)-*N*-  
methylamino]thiazol-2-yl)methyl]-1,3,2-dioxaphosphinane-2-oxide;
- 2-[1-Hydroxy-1-(4-[2-{4-(4-trifluoromethylphenyl)phenoxy}ethoxy]thiazol-2-  
yl)methyl]-1,3,2-dioxaphosphinane-2-oxide;
- 2-[1-Hydroxy-1-(4-[*N*-(2-{4-(4-trifluoromethylphenyl)phenoxy}ethyl)-*N*-  
20 methylamino]thiazol-2-yl)methyl]-1,3,2-dioxaphosphinane-2-oxide;
- 2-[1-Hydroxy-1-(4-[3-{4-(4-trifluoromethylphenyl)phenoxy}-1-oxoprop-1-yl]thiazol-  
2-yl)methyl]-1,3,2-dioxaphosphinane-2-oxide;
- 2-[1-Hydroxy-1-(4-[2-{1-[4-(2-trifluoromethylphenyl)phenylmethyl]-3-  
hexylureido}ethyl]thiazol-2-yl)methyl]-1,3,2-dioxaphosphinane-2-oxide;

- 2-[1-Hydroxy-1-(4-[2-{1-butyl-3-(5-methoxypyrid-2-yl)ureido}ethyl]thiazol-2-yl)methyl]-1,3,2-dioxaphosphinane-2-oxide;
- 2-[1-Hydroxy-1-(4-[3-{4-acetyl-3-hydroxy-2-propylphenoxy}propoxy]thiazol-2-yl)methyl]-1,3,2-dioxaphosphinane-2-oxide;
- 5 2-[1-Hydroxy-1-(4-[2-{4*H*-3-oxobenzo[1,4]oxazin-2-yl}ethoxy]thiazol-2-yl)methyl]-1,3,2-dioxaphosphinane-2-oxide;
- 2-[1-Hydroxy-1-(4-[3,*N*-phthalimidopropoxy]thiazol-2-yl)methyl]-1,3,2-dioxaphosphinane-2-oxide;
- 2-[1-Hydroxy-1-(4-[4,*N*-phthalimidobutoxy]thiazol-2-yl)methyl]-1,3,2-dioxaphosphinane-2-oxide;
- 10 2[1-(6-[2-{*N*-methyl-*N*-pyrid-2-ylamino}ethoxy]-3-methoxyquinolin-2-yl)-1-(2-oxido-1,3,2-dioxaphospholan-2-yl)methoxy]-1,3,2-dioxaphospholane-2-oxide;
- 2[1-(6-[*N*-(2-{*N*-methyl-*N*-pyrid-2-ylamino}ethyl)-*N*-methylamino]-3-methoxyquinolin-2-yl)-1-(2-oxido-1,3,2-dioxaphospholan-2-yl)methoxy]-1,3,2-dioxaphospholane-2-oxide;
- 15 2[1-(6-[3-{*N*-methyl-*N*-pyrid-2-ylamino}-1-oxoprop-1-yl]-3-methoxyquinolin-2-yl)-1-(2-oxido-1,3,2-dioxaphospholan-2-yl)methoxy]-1,3,2-dioxaphospholane-2-oxide;
- 2[1-(6-[2-{5-methyl-2-phenyloxazol-4-yl}ethoxy]-3-methoxyquinolin-2-yl)-1-(2-oxido-1,3,2-dioxaphospholan-2-yl)methoxy]-1,3,2-dioxaphospholane-2-oxide;
- 20 2[1-(6-[*N*-(2-{5-methyl-2-phenyloxazol-4-yl}ethyl)-*N*-methylamino]-3-methoxyquinolin-2-yl)-1-(2-oxido-1,3,2-dioxaphospholan-2-yl)methoxy]-1,3,2-dioxaphospholane-2-oxide;
- 2[1-(6-[2-{5-methyl-2-phenylthiazol-4-yl}ethoxy]-3-methoxyquinolin-2-yl)-1-(2-oxido-1,3,2-dioxaphospholan-2-yl)methoxy]-1,3,2-dioxaphospholane-2-oxide;
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- 2[1-(6-[3-{5-methyl-2-phenylthiazol-4-yl}-1-oxoprop-1-yl]-3-methoxyquinolin-2-yl)-1-(2-oxido-1,3,2-dioxaphospholan-2-yl)methoxy]-1,3,2-dioxaphospholane-2-oxide;
- 2[1-(6-[2-{5-methyl-2-pyrid-4-yloxazol-4-yl}ethoxy]-3-methoxyquinolin-2-yl)-1-(2-oxido-1,3,2-dioxaphospholan-2-yl)methoxy]-1,3,2-dioxaphospholane-2-oxide;
- 2[1-(6-[2-{5-methyl-2-pyrid-4-ylthiazol-4-yl}ethoxy]-3-methoxyquinolin-2-yl)-1-(2-oxido-1,3,2-dioxaphospholan-2-yl)methoxy]-1,3,2-dioxaphospholane-2-oxide;
- 2[1-(6-[3-{5-methyl-2-pyrid-4-yloxazol-4-yl}-1-oxoprop-1-yl]-3-methoxyquinolin-2-yl)-1-(2-oxido-1,3,2-dioxaphospholan-2-yl)methoxy]-1,3,2-dioxaphospholane-2-oxide;
- 2[1-(6-[*N*-(2-{5-methyl-2-pyrid-4-ylthiazol-4-yl}ethyl)-*N*-methylamino]-3-methoxyquinolin-2-yl)-1-([4*R*]-methyl-2-oxido-1,3,2-dioxaphospholan-2-yl)methoxy]-[4*R*]-methyl-1,3,2-dioxaphospholane-2-oxide;
- 2[1-(6-[2-{4-(4-trifluoromethylphenyl)phenoxy}ethoxy]-3-methoxyquinolin-2-yl)-1-([4*R*]-methyl-2-oxido-1,3,2-dioxaphospholan-2-yl)methoxy]-[4*R*]-methyl-1,3,2-dioxaphospholane-2-oxide;
- 2[1-(6-[*N*-(2-{4-(4-trifluoromethylphenyl)phenoxy}ethyl)-*N*-methylamino]-3-methoxyquinolin-2-yl)-1-([4*R*]-methyl-2-oxido-1,3,2-dioxaphospholan-2-yl)methoxy]-[4*R*]-methyl-1,3,2-dioxaphospholane-2-oxide;
- 2[1-(6-[3-{4-(4-trifluoromethylphenyl)phenoxy}-1-oxoprop-1-yl]-3-methoxyquinolin-2-yl)-1-([4*R*]-methyl-2-oxido-1,3,2-dioxaphospholan-2-yl)methoxy]-[4*R*]-methyl-1,3,2-dioxaphospholane-2-oxide;
- 2[1-(6-[2-{1-[4-(2-trifluoromethylphenyl)phenylmethyl]-3-hexylureido}ethyl]-3-methoxyquinolin-2-yl)-1-([4*R*]-methyl-2-oxido-1,3,2-dioxaphospholan-2-yl)methoxy]-[4*R*]-methyl-1,3,2-dioxaphospholane-2-oxide;

- 2[1-(6-[2-{1-butyl-3-(5-methoxypyrid-2-yl)ureido}ethyl]-3-methoxyquinolin-2-yl)-1-  
 ([4R]-methyl-2-oxido-1,3,2-dioxaphospholan-2-yl)methoxy]-[4R]-methyl-1,3,2-  
 dioxaphospholane-2-oxide;
- 2[1-(6-[3-{4-acetyl-3-hydroxy-2-propylphenoxy}propoxy]-3-methoxyquinolin-2-yl)-  
 5 1-([4R]-methyl-2-oxido-1,3,2-dioxaphospholan-2-yl)methoxy]-[4R]-methyl-  
 1,3,2-dioxaphospholane-2-oxide;
- 2[1-(6-[2-{4*H*-3-oxobenzo[1,4]oxazin-2-yl}ethoxy]-3-methoxyquinolin-2-yl)-1-  
 ([4R]-methyl-2-oxido-1,3,2-dioxaphospholan-2-yl)methoxy]-[4R]-methyl-1,3,2-  
 dioxaphospholane-2-oxide;
- 10 2[1-(6-[3,*N*-phthalimidopropoxy]-3-methoxyquinolin-2-yl)-1-([4R]-methyl-2-oxido-  
 1,3,2-dioxaphospholan-2-yl)methoxy]-[4R]-methyl-1,3,2-dioxaphospholane-2-  
 oxide;
- 2[1-(6-[4,*N*-phthalimidobutoxy]-3-methoxyquinolin-2-yl)-1-([4R]-methyl-2-oxido-  
 1,3,2-dioxaphospholan-2-yl)methoxy]-[4R]-methyl-1,3,2-dioxaphospholane-2-  
 15 oxide;
- 2[1-(5-[2-{*N*-methyl-*N*-pyrid-2-ylamino}ethoxy]thien-2-yl)-1-([4S]-methyl-2-oxido-  
 1,3,2-dioxaphospholan-2-yl)methoxy]-[4S]-methyl-1,3,2-dioxaphospholane-2-  
 oxide;
- 2[1-(5-[*N*-(2-{*N*-methyl-*N*-pyrid-2-ylamino}ethyl)-*N*-methylanino]thien-2-yl)-1-  
 20 ([4S]-methyl-2-oxido-1,3,2-dioxaphospholan-2-yl)methoxy]-[4S]-methyl-1,3,2-  
 dioxaphospholane-2-oxide;
- 2[1-(5-[3-{*N*-methyl-*N*-pyrid-2-ylamino}-1-oxoprop-1-yl]thien-2-yl)-1-([4S]-methyl-  
 2-oxido-1,3,2-dioxaphospholan-2-yl)methoxy]-[4S]-methyl-1,3,2-  
 dioxaphospholane-2-oxide;

- 2[1-(5-[2-{5-methyl-2-phenyloxazol-4-yl}ethoxy]thien-2-yl)-1-([4S]-methyl-2-oxido-1,3,2-dioxaphospholan-2-yl)methoxy]- [4S]-methyl-1,3,2-dioxaphospholane-2-oxide;
- 5 2[1-(5-[*N*-(2-{5-methyl-2-phenyloxazol-4-yl}ethyl)-*N*-methylamino]thien-2-yl)-1-([4S]-methyl-2-oxido-1,3,2-dioxaphospholan-2-yl)methoxy]- [4S]-methyl-1,3,2-dioxaphospholane-2-oxide;
- 2[1-(5-[2-{5-methyl-2-phenylthiazol-4-yl}ethoxy]thien-2-yl)-1-([4S]-methyl-2-oxido-1,3,2-dioxaphospholan-2-yl)methoxy]- [4S]-methyl-1,3,2-dioxaphospholane-2-oxide;
- 10 2[1-(5-[3-{5-methyl-2-phenylthiazol-4-yl}-1-oxoprop-1-yl]thien-2-yl)-1-([4S]-methyl-2-oxido-1,3,2-dioxaphospholan-2-yl)methoxy]- [4S]-methyl-1,3,2-dioxaphospholane-2-oxide;
- 2[1-(5-[2-{5-methyl-2-pyrid-4-yloxazol-4-yl}ethoxy]thien-2-yl)-1-([4S]-methyl-2-oxido-1,3,2-dioxaphospholan-2-yl)methoxy]- [4S]-methyl-1,3,2-dioxaphospholane-2-oxide;
- 15 2[1-(5-[2-{5-methyl-2-pyrid-4-ylthiazol-4-yl}ethoxy]thien-2-yl)-1-([4S]-methyl-2-oxido-1,3,2-dioxaphospholan-2-yl)methoxy]- [4S]-methyl-1,3,2-dioxaphospholane-2-oxide;
- 2[1-(5-[3-{5-methyl-2-pyrid-4-yloxazol-4-yl}-1-oxoprop-1-yl]thien-2-yl)-1-([4S]-methyl-2-oxido-1,3,2-dioxaphospholan-2-yl)methoxy]- [4S]-methyl-1,3,2-dioxaphospholane-2-oxide;
- 20 2[1-(5-[*N*-(2-{5-methyl-2-pyrid-4-ylthiazol-4-yl}ethyl)-*N*-methylamino]thien-2-yl)-1-(4,5-dimethyl-2-oxido-1,3,2-dioxaphospholan-2-yl)methoxy]-4,5-dimethyl-1,3,2-dioxaphospholane-2-oxide;

- 2[1-(5-[2-{4-(4-trifluoromethylphenyl)phenoxy}ethoxy]thien-2-yl)-1-(4,5-dimethyl-  
2-oxido-1,3,2-dioxaphospholan-2-yl)methoxy]-4,5-dimethyl1,3,2-  
dioxaphospholane-2-oxide;
- 2[1-(5-[*N*-(2-{4-(4-trifluoromethylphenyl)phenoxy}ethyl)-*N*-methylamino]thien-2-  
5 yl)-1-(4,5-dimethyl-2-oxido-1,3,2-dioxaphospholan-2-yl)methoxy]-4,5-  
dimethyl1,3,2-dioxaphospholane-2-oxide;
- 2[1-(5-[3-{4-(4-trifluoromethylphenyl)phenoxy}-1-oxoprop-1-yl]thien-2-yl)-1-(4,5-  
dimethyl-2-oxido-1,3,2-dioxaphospholan-2-yl)methoxy]-4,5-dimethyl1,3,2-  
dioxaphospholane-2-oxide;
- 10 2[1-(5-[2-{1-[4-(2-trifluoromethylphenyl)phenylmethyl]-3-hexylureido}ethyl]thien-2-  
yl)-1-(4,5-dimethyl-2-oxido-1,3,2-dioxaphospholan-2-yl)methoxy]-4,5-  
dimethyl1,3,2-dioxaphospholane-2-oxide;
- 2[1-(5-[2-{1-butyl-3-(5-methoxypyrid-2-yl)ureido}ethyl]thien-2-yl)-1-(4,5-dimethyl-  
2-oxido-1,3,2-dioxaphospholan-2-yl)methoxy]-4,5-dimethyl1,3,2-  
15 dioxaphospholane-2-oxide;
- 2[1-(5-[3-{4-acetyl-3-hydroxy-2-propylphenoxy}propoxy]thien-2-yl)-1-(4,5-dimethyl-  
2-oxido-1,3,2-dioxaphospholan-2-yl)methoxy]-4,5-dimethyl1,3,2-  
dioxaphospholane-2-oxide;
- 2[1-(5-[2-{4*H*-3-oxobenzo[1,4]oxazin-2-yl}ethoxy]thien-2-yl)-1-(4,5-dimethyl-2-  
20 oxido-1,3,2-dioxaphospholan-2-yl)methoxy]-4,5-dimethyl1,3,2-  
dioxaphospholane-2-oxide;
- 2[1-(5-[3,*N*-phthalimidopropoxy]thien-2-yl)-1-(4,5-dimethyl-2-oxido-1,3,2-  
dioxaphospholan-2-yl)methoxy]-4,5-dimethyl1,3,2-dioxaphospholane-2-oxide;
- 2[1-(5-[4,*N*-phthalimidobutoxy]thien-2-yl)-1-(4,5-dimethyl-2-oxido-1,3,2-  
25 dioxaphospholan-2-yl)methoxy]-4,5-dimethyl1,3,2-dioxaphospholane-2-oxide;



- 2[1-(4-[2-{*N*-methyl-*N*-pyrid-2-ylamino}ethoxy]-3-fluorophenyl)-1-(2-oxido-1,3,2-dioxaphosphinan-2-yl)methoxy]-1,3,2-dioxaphosphinane-2-oxide;
- 2[1-(4-[*N*-(2-{*N*-methyl-*N*-pyrid-2-ylamino}ethyl)-*N*-methylaminocarbonyl]-3-fluorophenyl)-1-(2-oxido-1,3,2-dioxaphosphinan-2-yl)methoxy]-1,3,2-dioxaphosphinane-2-oxide;
- 5 2[1-(4-[3-{*N*-methyl-*N*-pyrid-2-ylamino}-1-oxoprop-1-yl]-3-fluorophenyl)-1-(2-oxido-1,3,2-dioxaphosphinan-2-yl)methoxy]-1,3,2-dioxaphosphinane-2-oxide;
- 2[1-(4-[2-{5-methyl-2-phenyloxazol-4-yl}ethoxy]-3-fluorophenyl)-1-(2-oxido-1,3,2-dioxaphosphinan-2-yl)methoxy]-1,3,2-dioxaphosphinane-2-oxide;
- 10 1-(4-[*N*-(2-{5-methyl-2-phenyloxazol-4-yl}ethyl)-*N*-methylaminocarbonyl]-3-fluorophenyl)-1,1-bis(2-oxido-1,3,2-dioxaphospholan-2-yl)methane;
- 1-(4-[2-{5-methyl-2-phenylthiazol-4-yl}ethoxy]-3-fluorophenyl)-1,1-bis(2-oxido-1,3,2-dioxaphospholan-2-yl)methane;
- 1-(4-[3-{5-methyl-2-phenylthiazol-4-yl}-1-oxoprop-1-yl]-3-fluorophenyl)-1,1-bis(2-oxido-1,3,2-dioxaphospholan-2-yl)methane;
- 15 1-(4-[2-{5-methyl-2-pyrid-4-yloxazol-4-yl}ethoxy]-3-fluorophenyl)-1,1-bis(2-oxido-1,3,2-dioxaphospholan-2-yl)methane;
- 1-(4-[2-{5-methyl-2-pyrid-4-ylthiazol-4-yl}ethoxy]-3-fluorophenyl)-1,1-bis(4,5-dimethyl-2-oxido-1,3,2-dioxaphospholan-2-yl)methane;
- 20 1-(4-[3-{5-methyl-2-pyrid-4-yloxazol-4-yl}-1-oxoprop-1-yl]-3-fluorophenyl)-1,1-bis(2-oxido-1,3,2-dioxaphosphinan-2-yl)methane;
- 1-(4-[*N*-(2-{5-methyl-2-pyrid-4-ylthiazol-4-yl}ethyl)-*N*-methylaminocarbonyl]-3-fluorophenyl)-1,1-bis(4,5-dimethyl-2-oxido-1,3,2-dioxaphospholan-2-yl)methane;
- 1-(4-[2-{4-(4-trifluoromethylphenyl)phenoxy}ethoxy]-3-fluorophenyl)-1,1-bis(2-oxido-1,3,2-dioxaphosphinan-2-yl)methane;
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- 1-(4-[*N*-(2-{4-(4-trifluoromethylphenyl)phenoxy}ethyl)-*N*-methylaminocarbonyl]-3-fluorophenyl)-1,1-bis(4,5-dimethyl-2-oxido-1,3,2-dioxaphospholan-2-yl)methane;
- 1-(4-[3-{4-(4-trifluoromethylphenyl)phenoxy}-1-oxoprop-1-yl]-3-fluorophenyl)-1,1-bis(2-oxido-1,3,2-dioxaphosphinan-2-yl)methane;
- 5 1-(4-[2-{1-[4-(2-trifluoromethylphenyl)phenylmethyl]-3-hexylureido}ethyl]-3-fluorophenyl)-1,1-bis(4,5-dimethyl-2-oxido-1,3,2-dioxaphospholan-2-yl)methane;
- 1-(4-[2-{1-butyl-3-(5-methoxypyrid-2-yl)ureido}ethyl]-3-fluorophenyl)-1,1-bis(2-oxido-1,3,2-dioxaphosphinan-2-yl)methane;
- 2-(4-[3-{4-acetyl-3-hydroxy-2-propylphenoxy}propoxy]-3-fluorophenyl)-1,2-bis(2-oxido-1,3,2-dioxaphospholan-2-yl)ethane;
- 10 2-(4-[2-{4*H*-3-oxobenzo[1,4]oxazin-2-yl}ethoxy]-3-fluorophenyl)-1,2-bis([4*R*]-methyl-2-oxido-1,3,2-dioxaphospholan-2-yl)ethane;
- 2-(4-[3,*N*-phthalimidopropoxy]-3-fluorophenyl)-1,2-bis(2-oxido-1,3,2-dioxaphospholan-2-yl)ethane;
- 15 2-(4-[4,*N*-phthalimidobutoxy]-3-fluorophenyl)-1,2-bis([4*R*]-methyl-2-oxido-1,3,2-dioxaphospholan-2-yl)ethane;
- 2-(3-[3-{*N*-methyl-*N*-pyrid-2-ylamino}propoxy]-4-fluorophenyl)-1,2-bis(2-oxido-1,3,2-dioxaphospholan-2-yl)ethane;
- 2-(3-[*N*-(3-{*N*-methyl-*N*-pyrid-2-ylamino}propyl)-*N*-methylamino]-4-fluorophenyl)-1,2-bis([4*R*]-methyl-2-oxido-1,3,2-dioxaphospholan-2-yl)ethane;
- 20 2-(3-[3-{*N*-methyl-*N*-pyrid-2-ylamino}-1-oxoprop-1-ylamino]-4-fluorophenyl)-1,2-bis(2-oxido-1,3,2-dioxaphospholan-2-yl)ethane;
- 2-(3-[3-{5-methyl-2-phenyloxazol-4-yl}propoxy]-4-fluorophenyl)-1,2-bis([4*R*]-methyl-2-oxido-1,3,2-dioxaphospholan-2-yl)ethane;

- 2-(3-[*N*-(2-{5-methyl-2-phenyloxazol-4-yl}ethyl)-*N*-methylaminocarbonyl]-4-methoxyphenyl)-1,1-bis(4,5-dimethyl-2-oxido-1,3,2-dioxaphospholan-2-yl)ethane;
- 2-(3-[3-{5-methyl-2-phenylthiazol-4-yl}propoxy]-4-fluorophenyl)-1,1-bis(2-oxido-1,3,2-dioxaphosphinan-2-yl)ethane;
- 2-(3-[3-{5-methyl-2-phenylthiazol-4-yl}-1-oxoprop-1-yl]-4-fluorophenyl)-1,1-bis(4,5-dimethyl-2-oxido-1,3,2-dioxaphospholan-2-yl)ethane;
- 2-(3-[4-{5-methyl-2-pyrid-4-yloxazol-4-yl}butoxy]-4-fluorophenyl)-1,1-bis(2-oxido-1,3,2-dioxaphosphinan-2-yl)ethane;
- 2-(3-[3-{5-methyl-2-pyrid-4-ylthiazol-4-yl}propoxy]-4-fluorophenyl)-1,1-bis(4,5-dimethyl-2-oxido-1,3,2-dioxaphospholan-2-yl)ethane;
- 2-(3-[3-{5-methyl-2-pyrid-4-yloxazol-4-yl}-1-oxoprop-1-ylthio]-4-fluorophenyl)-1,1-bis(2-oxido-1,3,2-dioxaphosphinan-2-yl)ethane;
- 2-(3-[*N*-(3-{5-methyl-2-pyrid-4-ylthiazol-4-yl}propyl)-*N*-methylamino]-4-fluorophenyl)-1,1-bis(4,5-dimethyl-2-oxido-1,3,2-dioxaphospholan-2-yl)ethane;
- 2-(3-[3-{4-(4-trifluoromethylphenyl)phenoxy}propoxy]-4-fluorophenyl)-1,1-bis(2-oxido-1,3,2-dioxaphosphinan-2-yl)ethane;
- 1-[*N*-(3-[*N*-(3-{4-(4-trifluoromethylphenyl)phenoxy}propyl)-*N*-methylamino]-4-fluorophenyl)amino]-1,1-bis(2-oxido-1,3,2-dioxaphospholan-2-yl)methane;
- 1-[*N*-(3-[4-{4-(4-trifluoromethylphenyl)phenoxy}-1-oxobut-1-yl]-4-fluorophenyl)amino]-1,1-bis([4*R*]-methyl-2-oxido-1,3,2-dioxaphospholan-2-yl)methane;
- 1-[*N*-(3-[2-{1-[4-(2-trifluoromethylphenyl)phenylmethyl]-3-hexylureido}ethyl]-4-fluorophenyl)amino]-1,1-bis(2-oxido-1,3,2-dioxaphospholan-2-yl)methane;

- 1-[*N*-(3-[2-{1-butyl-3-(5-methoxypyrid-2-yl)ureido}ethyl]-4-fluorophenyl)amino]-  
1,1-bis([4*R*]-methyl-2-oxido-1,3,2-dioxaphospholan-2-yl)methane;
- 1-[*N*-(3-[4-{4-acetyl-3-hydroxy-2-propylphenoxy}butoxy]-4-fluorophenyl)amino]-  
1,1-bis(2-oxido-1,3,2-dioxaphospholan-2-yl)methane;
- 5 1-[*N*-(3-[3-{4*H*-3-oxobenzo[1,4]oxazin-2-yl}propoxy]-4-fluorophenyl)amino]-1,1-  
bis([4*R*]-methyl-2-oxido-1,3,2-dioxaphospholan-2-yl)methane;
- 1-[*N*-(3-[3,*N*-phthalimidopropoxy]-4-fluorophenyl)amino]-1,1-bis(2-oxido-1,3,2-  
dioxaphospholan-2-yl)methane;
- 1-[*N*-(3-[4,*N*-phthalimidobutoxy]-4-fluorophenyl)amino]-1,1-bis([4*R*]-methyl-2-  
10 oxido-1,3,2-dioxaphospholan-2-yl)methane;
- 1-[*N*-(6-[2-{*N*-methyl-*N*-pyrid-2-ylamino}ethoxy]indol-2-yl)amino]-1,1-bis(2-oxido-  
1,3,2-dioxaphosphinan-2-yl)methane;
- 1-[*N*-(6-[*N*-(2-{*N*-methyl-*N*-pyrid-2-ylamino}ethyl)-*N*-methylamino]indol-2-  
yl)amino]-1,1-bis(2-oxido-1,3,2-dioxaphosphinan-2-yl)methane;
- 15 1-[*N*-(6-[3-{*N*-methyl-*N*-pyrid-2-ylamino}-1-oxoprop-1-yl]indol-2-yl)amino]-1,1-  
bis(2-oxido-1,3,2-dioxaphosphinan-2-yl)methane;
- 1-[*N*-(6-[2-{5-methyl-2-phenyloxazol-4-yl}ethoxy] indol-2-yl)amino]-1,1-bis(2-  
oxido-1,3,2-dioxaphosphinan-2-yl)methane;
- 2-[1-(Diethoxyphosphinyloxy)-1-(6-[*N*-(2-{5-methyl-2-phenyloxazol-4-yl}ethyl)-*N*-  
20 methylamino] indol-2-yl)methyl]-1,3,2-dioxaphospholane-2-oxide;
- 2-[1-(Diethoxyphosphinyloxy)-1-(6-[2-{5-methyl-2-phenylthiazol-4-yl}ethoxy]indol-  
2-yl)methyl]-1,3,2-dioxaphospholane-2-oxide;
- 2-[1-(Diethoxyphosphinyloxy)-1-(6-[3-{5-methyl-2-phenylthiazol-4-yl}-1-oxoprop-1-  
yl]indol-2-yl)methyl]-1,3,2-dioxaphospholane-2-oxide;

- 2-[1-(Diethoxyphosphinyloxy)-1-(6-[2-{5-methyl-2-pyrid-4-yloxazol-4-yl}ethoxy]indol-2-yl)methyl]-1,3,2-dioxaphospholane-2-oxide;
- 2-[1-(Diethoxyphosphinyloxy)-1-(6-[2-{5-methyl-2-pyrid-4-ylthiazol-4-yl}ethoxy]indol-2-yl)methyl]-1,3,2-dioxaphosphinane-2-oxide;
- 5 2-[1-(Diethoxyphosphinyloxy)-1-(6-[3-{5-methyl-2-pyrid-4-yloxazol-4-yl}-1-oxoprop-1-yl]indol-2-yl)methyl]-1,3,2-dioxaphosphinane-2-oxide;
- 2-[1-(Diethoxyphosphinyloxy)-1-(6-[*N*-(2-{5-methyl-2-pyrid-4-ylthiazol-4-yl}ethyl)-*N*-methylamino]indol-2-yl)methyl]-1,3,2-dioxaphosphinane-2-oxide;
- 2-[1-(Diethoxyphosphinyloxy)-1-(6-[2-{4-(4-trifluoromethylphenyl)phenoxy}ethoxy]indol-2-yl)methyl]-1,3,2-dioxaphosphinane-2-oxide;
- 10 2[1-(6-[*N*-(2-{4-(4-trifluoromethylphenyl)phenoxy}ethyl)-*N*-methylamino]indol-2-yl)-1-(diethoxyphosphinyl)methoxy]-4[*S*]-methyl-1,3,2-dioxaphospholane-2-oxide;
- 2[1-(6-[3-{4-(4-trifluoromethylphenyl)phenoxy}-1-oxoprop-1-yl]indol-2-yl)-1-(diethoxyphosphinyl)methoxy]-4,5-dimethyl-1,3,2-dioxaphospholane-2-oxide;
- 15 2[1-(6-[2-{1-[4-(2-trifluoromethylphenyl)phenylmethyl]-3-hexylureido}ethyl]indol-2-yl)-1-(diethoxyphosphinyl)methoxy]-4[*S*]-methyl-1,3,2-dioxaphospholane-2-oxide;
- 2[1-(6-[2-{1-[4-(2-trifluoromethylphenyl)phenylmethyl]-3-hexylureido}ethyl]indol-2-yl)-1-(diethoxyphosphinyl)methoxy]-4,5-dimethyl-1,3,2-dioxaphospholane-2-oxide;
- 20 2[1-(6-[3-{4-acetyl-3-hydroxy-2-propylphenoxy}propoxy]indol-2-yl)-1-(diethoxyphosphinyl)methoxy]-4[*S*]-methyl-1,3,2-dioxaphospholane-2-oxide;
- 2[1-(6-[2-{4*H*-3-oxobenzo[1,4]oxazin-2-yl}ethoxy]indol-2-yl)-1-(diethoxyphosphinyl)methoxy]-4,5-dimethyl-1,3,2-dioxaphospholane-2-oxide;
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- 2[1-(6-[2-{1-butyl-3-(5-methoxypyrid-2-yl)ureido}ethyl]indol-2-yl)-1-(diethoxyphosphinyl)methoxy]-4[S]-methyl-1,3,2-dioxaphospholane-2-oxide;
- 2[1-(6-[3,*N*-phthalimidopropoxy]indol-2-yl)-1-(diethoxyphosphinyl)methoxy]-4,5-dimethyl-1,3,2-dioxaphospholane-2-oxide;
- 5 2[1-(6-[4,*N*-phthalimidobutoxy]indol-2-yl)-1-(diethoxyphosphinyl)methyl]-4[R]-methyl-1,3,2-dioxaphospholane-2-oxide;
- 2[1-(5-[2-{*N*-methyl-*N*-pyrid-2-ylamino}ethoxy]pyrid-2-yl)-1-(diethoxyphosphinyl)methyl]-4[R]-methyl-1,3,2-dioxaphospholane-2-oxide;
- 2[1-(5-[*N*-(2-{*N*-methyl-*N*-pyrid-2-ylamino}ethyl)-*N*-methylamino]pyrid-2-yl)-1-(diethoxyphosphinyl)methyl]-4[R]-methyl-1,3,2-dioxaphospholane-2-oxide;
- 10 2[1-(5-[3-{*N*-methyl-*N*-pyrid-2-ylamino}-1-oxoprop-1-yl]pyrid-2-yl)-1-(diethoxyphosphinyl)methyl]-4[R]-methyl-1,3,2-dioxaphospholane-2-oxide;
- 2[1-(5-[2-{5-methyl-2-phenyloxazol-4-yl}ethoxy]pyrid-2-yl)-1-(diethoxyphosphinyl)methyl]-1,3,2-dioxaphosphinane-2-oxide;
- 15 2[1-(5-[*N*-(2-{5-methyl-2-phenyloxazol-4-yl}ethyl)-*N*-methylamino]pyrid-2-yl)-1-(diethoxyphosphinyl)methyl]-1,3,2-dioxaphosphinane-2-oxide;
- 2[1-(5-[*N*-(2-{5-methyl-2-phenyloxazol-4-yl}ethyl)-*N*-methylamino]pyrid-2-yl)-1-(diethoxyphosphinyl)methyl]-1,3,2-dioxaphosphinane-2-oxide;
- 2[1-(5-[2-{5-methyl-2-phenylthiazol-4-yl}ethoxy]pyrid-2-yl)-1-(diethoxyphosphinyl)methyl]-1,3,2-dioxaphosphinane-2-oxide;
- 20 2[1-(5-[3-{5-methyl-2-phenylthiazol-4-yl}-1-oxoprop-1-yl]pyrid-2-yl)-2-(diethoxyphosphinyl)eth-1-yl]-4,5-dimethyl-1,3,2-dioxaphospholane-2-oxide;
- 2[1-(5-[2-{5-methyl-2-pyrid-4-yloxazol-4-yl}ethoxy]pyrid-2-yl)-2-(diethoxyphosphinyl)eth-1-yl]-1,3,2-dioxaphosphinane-2-oxide;

- 2[1-(5-[2-{5-methyl-2-pyrid-4-ylthiazol-4-yl}ethoxy]pyrid-2-yl)-2-(diethoxyphosphinyl)eth-1-yl]-4,5-dimethyl-1,3,2-dioxaphospholane-2-oxide;
- 2[1-(5-[3-{5-methyl-2-pyrid-4-ylloxazol-4-yl}-1-oxoprop-1-yl]pyrid-2-yl)-2-(diethoxyphosphinyl)eth-1-yl]-1,3,2-dioxaphosphinane-2-oxide;
- 5 2[1-(5-[*N*-(2-{5-methyl-2-pyrid-4-ylthiazol-4-yl}ethyl)-*N*-methylamino]pyrid-2-yl)-2-(diethoxyphosphinyl)eth-1-yl]-4,5-dimethyl-1,3,2-dioxaphospholane-2-oxide;
- 2[1-(5-[2-{4-(4-trifluoromethylphenyl)phenoxy}ethoxy]-pyrid-2-yl)-2-(diethoxyphosphinyl)eth-1-yl]-1,3,2-dioxaphosphinane-2-oxide;
- 2[1-(5-[*N*-(2-{4-(4-trifluoromethylphenyl)phenoxy}ethyl)-*N*-methylamino]pyrid-2-yl)-2-(diethoxyphosphinyl)eth-1-yl]-4,5-dimethyl-1,3,2-dioxaphospholane-2-oxide;
- 10 2[1-(5-[3-{4-(4-trifluoromethylphenyl)phenoxy}-1-oxoprop-1-yl]-pyrid-2-yl)-2-(diethoxyphosphinyl)eth-1-yl]-1,3,2-dioxaphosphinane-2-oxide;
- 2[2-(5-[2-{1-[4-(2-trifluoromethylphenyl)phenylmethyl]-3-hexylureido}ethyl]pyrid-2-yl)-2-(diethoxyphosphinyl)eth-1-yl]-1,3,2-dioxaphospholane-2-oxide;
- 15 2[2-(5-[2-{1-butyl-3-(5-methoxypyrid-2-yl)ureido}ethyl]pyrid-2-yl)-2-(diethoxyphosphinyl)eth-1-yl]-4[R]-methyl-1,3,2-dioxaphospholane-2-oxide;
- 2[2-(5-[3-{4-acetyl-3-hydroxy-2-propylphenoxy}propoxy]pyrid-2-yl)-2-(diethoxyphosphinyl)eth-1-yl]-1,3,2-dioxaphospholane-2-oxide;
- 20 2[2-(5-[2-{4*H*-3-oxobenzo[1,4]oxazin-2-yl}ethoxy]pyrid-2-yl)-2-(diethoxyphosphinyl)eth-1-yl]-4[R]-methyl-1,3,2-dioxaphospholane-2-oxide;
- 2[2-(5-[3,*N*-phthalimidopropoxy]pyrid-2-yl)-2-(diethoxyphosphinyl)eth-1-yl]-1,3,2-dioxaphospholane-2-oxide;
- 2[2-(5-[4,*N*-phthalimidobutoxy]pyrid-2-yl)-2-(diethoxyphosphinyl)eth-1-yl]-4[R]-methyl-1,3,2-dioxaphospholane-2-oxide;
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- 2[2-(5-[2-{*N*-methyl-*N*-pyrid-2-ylamino}ethoxy]benzothien-2-yl)-2-(diethoxyphosphinyl)eth-1-yl]-1,3,2-dioxaphospholane-2-oxide;
- 2[2-(5-[*N*-(2-{*N*-methyl-*N*-pyrid-2-ylamino}ethyl)-*N*-methylamino]benzothien-2-yl)-2-(diethoxyphosphinyl)eth-1-yl]-4[R]-methyl-1,3,2-dioxaphospholane-2-oxide;
- 5 2[2-(5-[3-{*N*-methyl-*N*-pyrid-2-ylamino}-1-oxoprop-1-yl]benzothien-2-yl)-2-(diethoxyphosphinyl)eth-1-yl]-1,3,2-dioxaphosphinane-2-oxide;
- 2[2-(5-[2-{5-methyl-2-phenyloxazol-4-yl}ethoxy]benzothien-2-yl)-2-(diethoxyphosphinyl)eth-1-yl]-1,3,2-dioxaphosphinane-2-oxide;
- 2[2-(5-[*N*-(2-{5-methyl-2-phenyloxazol-4-yl}ethyl)-*N*-methylamino]benzothien-2-yl)-2-(diethoxyphosphinyl)eth-1-yl]-1,3,2-dioxaphosphinane-2-oxide;
- 10 2[2-(5-[2-{5-methyl-2-phenylthiazol-4-yl}ethoxy]benzothien-2-yl)-2-(diethoxyphosphinyl)eth-1-yl]-1,3,2-dioxaphosphinane-2-oxide;
- 2[2-(5-[3-{5-methyl-2-phenylthiazol-4-yl}-1-oxoprop-1-yl]benzothien-2-yl)-1-(diethoxyphosphinyl)eth-1-yl]-1,3,2-dioxaphospholane-2-oxide;
- 15 2[2-(5-[2-{5-methyl-2-pyrid-4-yloxazol-4-yl}ethoxy]benzothien-2-yl)-1-(diethoxyphosphinyl)eth-1-yl]-1,3,2-dioxaphospholane-2-oxide;
- 2[2-(5-[2-{5-methyl-2-pyrid-4-ylthiazol-4-yl}ethoxy]benzothien-2-yl)-1-(diethoxyphosphinyl)eth-1-yl]-1,3,2-dioxaphospholane-2-oxide;
- 2[2-(5-[3-{5-methyl-2-pyrid-4-yloxazol-4-yl}-1-oxoprop-1-yl]benzothien-2-yl)-1-(diethoxyphosphinyl)eth-1-yl]-1,3,2-dioxaphospholane-2-oxide;
- 20 *N,N,N',N'*-Tetramethyl-1 (5-[*N*-(2-{5-methyl-2-pyrid-4-ylthiazol-4-yl}ethyl)-*N*-methylamino]benzothien-2-yl)-1-hydroxymethylphosphondiamide;
- N,N'*-Diethyl 1-(5-[2-{4-(4-trifluoromethylphenyl)phenoxy}ethoxy]benzothien-2-yl)-1-hydroxymethylphosphondiamide;



- 2-[1-hydroxy-1-(5-[*N*-(2-{4-(4-trifluoromethylphenyl)phenoxy}ethyl)-*N*-methylamino]benzothien-2-yl)methyl]-[4*S*,5*S*]-dimethyl-1,3,2-diazaphospholidine-2-oxide;
- 2-[1-hydroxy-1-(5-[3-{4-(4-trifluoromethylphenyl)phenoxy}-1-oxoprop-1-yl]benzothien-2-yl)methyl]-1,3,5,5-tetramethyl-1,3,2-diazaphosphinane-2-oxide;
- 2-[1-hydroxy-1-(5-[2-{1-[4-(2-trifluoromethylphenyl)phenylmethyl]-3-hexylureido}ethyl]benzothien-2-yl)methyl]-[4*S*]-ethyl-1,3,2-oxazaphospholidine-2-oxide;
- 2-[1-hydroxy-1-(5-[2-{1-butyl-3-(5-methoxypyrid-2-yl)ureido}ethyl]benzothien-2-yl)methyl]-[4*R*]-methyl-1,3,2-oxazaphosphinane-2-oxide;
- N,N,N',N'*-Tetramethyl-1 (5-[3-{4-acetyl-3-hydroxy-2-propylphenoxy)propoxy]benzothien-2-yl)-1-hydroxymethylphosphondiamide;
- N,N'*-Diethyl 1-(5-[2-{4*H*-3-oxobenzo[1,4]oxazin-2-yl}ethoxy]benzothien-2-yl)-1-hydroxymethylphosphondiamide;
- 2-[1-hydroxy-1-(5-[3,*N*-phthalimidopropoxy]benzothien-2-yl)methyl]-[4*S*,5*S*]-dimethyl-1,3,2-diazaphospholidine-2-oxide;
- 2-[1-hydroxy-1-(5-[4,*N*-phthalimidobutoxy]benzothien-2-yl)methyl]-1,3,5,5-tetramethyl-1,3,2-diazaphosphinane-2-oxide;
- 2-[1-hydroxy-1-(4-[2-{*N*-methyl-*N*-pyrid-2-ylamino}ethoxy]thiazol-2-yl)methyl]-[4*S*]-ethyl-1,3,2-oxazaphospholidine-2-oxide;
- 2-[1-hydroxy-1-(4-[*N*-(2-{*N*-methyl-*N*-pyrid-2-ylamino}ethyl)-*N*-methylamino]thiazol-2-yl)methyl]-[4*R*]-methyl-1,3,2-oxazaphosphinane-2-oxide;
- N,N,N',N'*-Tetramethyl 1-(4-[3-{*N*-methyl-*N*-pyrid-2-ylamino}-1-oxoprop-1-yl]thiazol-2-yl)-1-(bis[*N,N*-dimethylamino]phosphoryloxy)methylphosphondiamide;

- N,N'*-Diethyl 1-(4-[2-{5-methyl-2-phenyloxazol-4-yl}ethoxy]thiazol-2-yl)-1-(bis[*N*-ethylamino]phosphoryloxy)methylphosphondiamide;
- 2-[1-{([4S,5S]-dimethyl-2-oxido-1,3,2-diazaphospholidin-2-yl)oxy}-1-(4-[*N*-(2-{5-methyl-2-phenyloxazol-4-yl}ethyl)-*N*-methylamino]thiazol-2-yl)methyl]-[4S,5S]-
- 5 dimethyl-1,3,2-diazaphospholidine-2-oxide;
- 2-[1-{(1,3,5,5-tetramethyl-2-oxido-1,3,2-diazaphosphinan-2-yl)oxy}-1-(4-[2-{5-methyl-2-phenylthiazol-4-yl}ethoxy]thiazol-2-yl)methyl]-1,3,5,5-tetramethyl-1,3,2-diazaphosphinane-2-oxide;
- 2-[1-{(4S)-ethyl-2-oxido-1,3,2-oxazaphospholidin-2-yl)oxy}-1-(4-[3-{5-methyl-2-phenylthiazol-4-yl}-1-oxoprop-1-yl]thiazol-2-yl)methyl]-[4S]-ethyl-1,3,2-
- 10 oxazaphospholidine-2-oxide;
- 2-[1-{([4R]methyl-1,3,2-oxazaphosphinan-2-yl)oxy}-1-(4-[2-{5-methyl-2-pyrid-4-yloxazol-4-yl}ethoxy]thiazol-2-yl)methyl]-[4R]methyl-1,3,2-oxazaphosphinane-2-oxide;
- 15 *N,N,N',N'*-Tetramethyl 1-(4-[2-{5-methyl-2-pyrid-4-ylthiazol-4-yl}ethoxy]thiazol-2-yl)-1-(bis[*N,N*-dimethylamino]phosphoryloxy)methylphosphondiamide;
- N,N'*-Diethyl 1-(4-[3-{5-methyl-2-pyrid-4-yloxazol-4-yl}-1-oxoprop-1-yl]thiazol-2-yl)-1-(bis[*N*-ethylamino]phosphoryloxy)methylphosphondiamide;
- 2-[1-{([4S,5S]-dimethyl-2-oxido-1,3,2-diazaphospholidin-2-yl)oxy}-1-(4-[*N*-(2-{5-
- 20 methyl-2-pyrid-4-ylthiazol-4-yl}ethyl)-*N*-methylamino]thiazol-2-yl)methyl]-[4S,5S]-dimethyl-1,3,2-diazaphospholidine-2-oxide;
- 2-[1-{(1,3,5,5-tetramethyl-2-oxido-1,3,2-diazaphosphinan-2-yl)oxy}-1-(4-[2-{4-(4-trifluoromethylphenyl)phenoxy}ethoxy]thiazol-2-yl)methyl]-1,3,5,5-tetramethyl-1,3,2-diazaphosphinane-2-oxide;

- 2-[1-{(4S)-ethyl-2-oxido-1,3,2-oxazaphospholidin-2-yl)oxy}-1-(4-[*N*-(2-{4-(4-trifluoromethylphenyl)phenoxy}ethyl)-*N*-methylamino]thiazol-2-yl)methyl]-[4S]-ethyl-1,3,2-oxazaphospholidine-2-oxide;
- 2-[1-{(4R)methyl-1,3,2-oxazaphosphinan-2-yl)oxy}-1-(4-[3-{4-(4-trifluoromethylphenyl)phenoxy}-1-oxoprop-1-yl]thiazol-2-yl)methyl]-[4R]methyl-1,3,2-oxazaphosphinane-2-oxide;
- 1-(4-[2-{1-[4-(2-trifluoromethylphenyl)phenylmethyl]-3-hexylureido}ethyl]thiazol-2-yl)-1,1-bis(bis[*N,N*-dimethylamino]phosphoryl)methane;
- 1-(4-[2-{1-butyl-3-(5-methoxypyrid-2-yl)ureido}ethyl]thiazol-2-yl)-1,1-bis(bis[*N*-ethylamino]phosphoryl)methane;
- 1-(4-[3-{4-acetyl-3-hydroxy-2-propylphenoxy}propoxy]thiazol-2-yl)-1,1-bis([4S,5S]-dimethyl-2-oxido-1,3,2-diazaphospholidin-2-yl)methane;
- 1-(4-[2-{4*H*-3-oxobenzo[1,4]oxazin-2-yl}ethoxy]thiazol-2-yl)-1,1-bis(1,3,5,5-tetramethyl-2-oxido-1,3,2-diazaphosphinan-2-yl)methane;
- 1-(4-[3,*N*-phthalimidopropoxy]thiazol-2-yl)-1,1-bis ([4S]-ethyl-2-oxido-1,3,2-oxazaphospholidin-2-yl)methane;
- 1-(4-[4,*N*-phthalimidobutoxy]thiazol-2-yl)-1,1-bis ([4R]methyl-2-oxido-1,3,2-oxazaphosphinan-2-yl)methane;
- 1-(6-[2-{*N*-methyl-*N*-pyrid-2-ylamino}ethoxy]-3-methoxyquinolin-2-yl)-1,1-bis(bis[*N,N*-dimethylamino]phosphoryl)methane;
- 1-(6-[*N*-(2-{*N*-methyl-*N*-pyrid-2-ylamino}ethyl)-*N*-methylamino]-3-methoxyquinolin-2-yl)-1,1-bis(bis[*N*-ethylamino]phosphoryl)methane;
- 1-(6-[3-{*N*-methyl-*N*-pyrid-2-ylamino}-1-oxoprop-1-yl]-3-methoxyquinolin-2-yl)-1,1-bis([4S,5S]-dimethyl-2-oxido-1,3,2-diazaphospholidin-2-yl)methane;

- 1-(6-[2-{5-methyl-2-phenyloxazol-4-yl}ethoxy]-3-methoxyquinolin-2-yl)-1,1-bis(1,3,5,5-tetramethyl-2-oxido-1,3,2-diazaphosphinan-2-yl)methane;
- 1-(6-[*N*-(2-{5-methyl-2-phenyloxazol-4-yl}ethyl)-*N*-methylamino]-3-methoxyquinolin-2-yl)-1,1-bis([4*S*]-ethyl-2-oxido-1,3,2-oxazaphospholidin-2-yl)methane;
- 5 1-(6-[2-{5-methyl-2-phenylthiazol-4-yl}ethoxy]-3-methoxyquinolin-2-yl)-1,1-bis([4*R*]-methyl-2-oxido-1,3,2-oxazaphosphinan-2-yl)methane;
- 1-(6-[3-{5-methyl-2-phenylthiazol-4-yl}-1-oxoprop-1-yl]-3-methoxyquinolin-2-yl)-1,2-bis(bis[*N,N*-dimethylamino]phosphoryl)ethane;
- 10 1-(6-[2-{5-methyl-2-pyrid-4-yloxazol-4-yl}ethoxy]-3-methoxyquinolin-2-yl)-1,2-bis(bis[*N*-ethylamino]phosphoryl)ethane;
- 1-(6-[2-{5-methyl-2-pyrid-4-ylthiazol-4-yl}ethoxy]-3-methoxyquinolin-2-yl)-1,2-bis([4*S*,5*S*]-dimethyl-2-oxido-1,3,2-diazaphospholidin-2-yl)ethane;
- 1-(6-[3-{5-methyl-2-pyrid-4-yloxazol-4-yl}-1-oxoprop-1-yl]-3-methoxyquinolin-2-yl)-1,2-bis(1,3,5,5-tetramethyl-2-oxido-1,3,2-diazaphosphinan-2-yl)ethane;
- 15 1-(6-[*N*-(2-{5-methyl-2-pyrid-4-ylthiazol-4-yl}ethyl)-*N*-methylamino]-3-methoxyquinolin-2-yl)-1,2-bis([4*S*]-ethyl-2-oxido-1,3,2-oxazaphospholidin-2-yl)ethane;
- 1-(6-[2-{4-(4-trifluoromethylphenyl)phenoxy}ethoxy]-3-methoxyquinolin-2-yl)-1,2-bis([4*R*]-methyl-2-oxido-1,3,2-oxazaphosphinan-2-yl)ethane;
- 20 1-(6-[*N*-(2-{4-(4-trifluoromethylphenyl)phenoxy}ethyl)-*N*-methylamino]-3-methoxyquinolin-2-yl)-1,2-bis(bis[*N,N*-dimethylamino]phosphoryl)ethane;
- 1-(6-[3-{4-(4-trifluoromethylphenyl)phenoxy}-1-oxoprop-1-yl]-3-methoxyquinolin-2-yl)-1,2-bis(bis[*N*-ethylamino]phosphoryl)ethane;

- 1-(6-[2-{1-[4-(2-trifluoromethylphenyl)phenylmethyl]-3-hexylureido}ethyl]-3-methoxyquinolin-2-yl)-1,2-bis([4S,5S]-dimethyl-2-oxido-1,3,2-diazaphospholidin-2-yl)ethane;
- 1-(6-[2-{1-butyl-3-(5-methoxypyrid-2-yl)ureido}ethyl]-3-methoxyquinolin-2-yl)-1,2-bis(1,3,5,5-tetramethyl-2-oxido-1,3,2-diazaphosphinan-2-yl)ethane;
- 1-(6-[3-{4-acetyl-3-hydroxy-2-propylphenoxy}propoxy]-3-methoxyquinolin-2-yl)-1,2-bis([4S]-ethyl-2-oxido-1,3,2-oxazaphospholidin-2-yl)ethane;
- 1-(6-[3,*N*-phthalimidopropoxy]-3-methoxyquinolin-2-yl)-1,2-bis([4R]methyl-2-oxido-1,3,2-oxazaphosphinan-2-yl)ethane;
- 2-(6-[4,*N*-phthalimidobutoxy]-3-methoxyquinolin-2-yl)-1,1-bis(bis[*N,N*-dimethylamino]phosphoryl)ethane;
- 2-(5-[2-{*N*-methyl-*N*-pyrid-2-ylamino}ethoxy]thien-2-yl)-1,1-bis(bis[*N*-ethylamino]phosphoryl)ethane;
- 2-(5-[*N*-(2-{*N*-methyl-*N*-pyrid-2-ylamino}ethyl)-*N*-methylamino]thien-2-yl)-1,1-bis([4S,5S]-dimethyl-2-oxido-1,3,2-diazaphospholidin-2-yl)ethane;
- 2-(5-[3-{*N*-methyl-*N*-pyrid-2-ylamino}-1-oxoprop-1-yl]thien-2-yl)-1,1-bis(1,3,5,5-tetramethyl-2-oxido-1,3,2-diazaphosphinan-2-yl)ethane;
- 2-(5-[2-{5-methyl-2-phenyloxazol-4-yl}ethoxy]thien-2-yl)-1,1-bis([4S]-ethyl-2-oxido-1,3,2-oxazaphospholidin-2-yl)ethane;
- 2-(5-[*N*-(2-{5-methyl-2-phenyloxazol-4-yl}ethyl)-*N*-methylamino]thien-2-yl)-1,1-bis([4R]methyl-2-oxido-1,3,2-oxazaphosphinan-2-yl)ethane;
- 2-(5-[2-{5-methyl-2-phenylthiazol-4-yl}ethoxy]thien-2-yl)-1,1-bis(bis[*N,N*-dimethylamino]phosphoryl)ethane;
- 2-(5-[3-{5-methyl-2-phenylthiazol-4-yl}-1-oxoprop-1-yl]thien-2-yl)-1,1-bis(bis[*N*-ethylamino]phosphoryl)ethane;

- 2-(5-[2-{5-methyl-2-pyrid-4-yloxazol-4-yl}ethoxy]thien-2-yl)-1,1-bis([4S,5S]-  
dimethyl-2-oxido-1,3,2-diazaphospholidin-2-yl)ethane;
- 2-(5-[2-{5-methyl-2-pyrid-4-ylthiazol-4-yl}ethoxy]thien-2-yl)-1,1-bis(1,3,5,5-  
tetramethyl-2-oxido-1,3,2-diazaphosphinan-2-yl)ethane;
- 5 2-(5-[3-{5-methyl-2-pyrid-4-yloxazol-4-yl}-1-oxoprop-1-yl]thien-2-yl)-1,1-bis ([4S]-  
ethyl-2-oxido-1,3,2-oxazaphospholidin-2-yl)ethane;
- 2-(5-[*N*-(2-{5-methyl-2-pyrid-4-ylthiazol-4-yl}ethyl)-*N*-methylamino]thien-2-yl)-1,1-  
bis ([4R]methyl-2-oxido-1,3,2-oxazaphosphinan-2-yl)ethane;
- 1-[*N*-(5-[2-{4-(4-trifluoromethylphenyl)phenoxy}ethoxy]thien-2-yl)amino]-1,1-  
10 bis(bis[*N,N*-dimethylamino]phosphoryl)methane;
- 1-[*N*-(5-[*N*-(2-{4-(4-trifluoromethylphenyl)phenoxy}ethyl)-*N*-methylamino]thien-2-  
yl)amino]-1,1-bis(bis[*N*-ethylamino]phosphoryl)methane;
- 1-[*N*-(5-[3-{4-(4-trifluoromethylphenyl)phenoxy}-1-oxoprop-1-yl]thien-2-yl)amino]-  
1,1-bis([4S,5S]-dimethyl-2-oxido-1,3,2-diazaphospholidin-2-yl)methane;
- 15 1-[*N*-(5-[2-{1-[4-(2-trifluoromethylphenyl)phenylmethyl]-3-hexylureido}ethyl]thien-  
2-yl)amino]-1,1-bis(1,3,5,5-tetramethyl-2-oxido-1,3,2-diazaphosphinan-2-  
yl)methane;
- 1-[*N*-(5-[2-{1-butyl-3-(5-methoxypyrid-2-yl)ureido}ethyl]thien-2-yl)amino]-1,1-bis  
([4S]-ethyl-2-oxido-1,3,2-oxazaphospholidin-2-yl)methane;
- 20 1-[*N*-(5-[3-{4-acetyl-3-hydroxy-2-propylphenoxy}propoxy]thien-2-yl)amino]-1,1-bis  
([4R]methyl-2-oxido-1,3,2-oxazaphosphinan-2-yl)methane;
- 1-[*N*-(5-[2-{4*H*-3-oxobenzo[1,4]oxazin-2-yl}ethoxy]thien-2-yl)amino]-1,1-  
bis(bis[*N,N*-dimethylamino]phosphoryl)methane;
- 1-[*N*-(5-[3,*N*-phthalimidopropoxy]thien-2-yl)amino]-1,1-bis(bis[*N*-  
25 ethylamino]phosphoryl)methane;

- 1-[*N*-(5-[4,*N*-phthalimidobutoxy]thien-2-yl)amino]-1,1-bis([4*S*,5*S*]-dimethyl-2-oxido-1,3,2-diazaphospholidin-2-yl)methane;
- 1-[*N*-(4-[2-{*N*-methyl-*N*-pyrid-2-ylamino}ethoxy]-3-fluorophenyl)amino]-1,1-bis(1,3,5,5-tetramethyl-2-oxido-1,3,2-diazaphosphinan-2-yl)methane;
- 5 1-[*N*-(4-[*N*-(2-{*N*-methyl-*N*-pyrid-2-ylamino}ethyl)-*N*-methylaminocarbonyl]-3-fluorophenyl)amino]-1,1-bis([4*S*]-ethyl-2-oxido-1,3,2-oxazaphospholidin-2-yl)methane;
- 1-[*N*-(4-[3-{*N*-methyl-*N*-pyrid-2-ylamino}-1-oxoprop-1-yl]-3-fluorophenyl)amino]-1,1-bis([4*R*]methyl-2-oxido-1,3,2-oxazaphosphinan-2-yl)methane;
- 10 2-[1-(Bis[*N*-ethylamino]phosphoryloxy)-1-(4-[2-{5-methyl-2-phenyloxazol-4-yl}ethoxy]-3-fluorophenyl)methyl]-[4*S*,5*S*]-dimethyl-1,3,2-diazaphospholidine-2-oxide;
- 2-[1-(Bis[*N*-ethylamino]phosphoryl)-1-(4-[*N*-(2-{5-methyl-2-phenyloxazol-4-yl}ethyl)-*N*-methylaminocarbonyl]-3-fluorophenyl)methoxy]-[4*S*,5*S*]-dimethyl-1,3,2-diazaphospholidine-2-oxide;
- 15 2-[1-(Bis[*N*-ethylamino]phosphoryl)-1-(4-[2-{5-methyl-2-phenylthiazol-4-yl}ethoxy]-3-fluorophenyl)methyl]-1,3,5,5-tetramethyl-1,3,2-diazaphosphinane-2-oxide;
- 2-[1-(Bis[*N*-ethylamino]phosphoryl)-2-(4-[3-{5-methyl-2-phenylthiazol-4-yl}-1-oxoprop-1-yl]-3-fluorophenyl)ethen-1-yl]-[4*S*]-ethyl-1,3,2-oxazaphospholidine-2-oxide;
- 20 2-[1-(Bis[*N*-ethylamino]phosphoryl)-2-(4-[2-{5-methyl-2-pyrid-4-yloxazol-4-yl}ethoxy]-3-fluorophenyl)eth-1-yl]-[4*R*]methyl-1,3,2-oxazaphosphinane-2-oxide;

- 2-[2-(Bis[*N*-ethylamino]phosphoryl)-2-(4-[2-{5-methyl-2-pyrid-4-ylthiazol-4-yl}ethoxy]-3-fluorophenyl)eth-1-yl]-1,3,5,5-tetramethyl-1,3,2-diazaphosphinane-2-oxide;
- 2-[2-(Bis[*N*-ethylamino]phosphoryl)-1-(4-[3-{5-methyl-2-pyrid-4-ylloxazol-4-yl}-1-oxoprop-1-yl]-3-fluorophenyl)eth-1-yl]-[4*S*]-ethyl-1,3,2-oxazaphospholidine-2-oxide;
- 2-[1-(Bis[*N*-ethylamino]phosphoryloxy)-1-(4-[*N*-(2-{5-methyl-2-pyrid-4-ylthiazol-4-yl}ethyl)-*N*-methylaminocarbonyl]-3-fluorophenyl)methyl]-[4*S*,5*S*]-dimethyl-1,3,2-diazaphospholidine-2-oxide;
- 2-[1-(Bis[*N*-ethylamino]phosphoryl)-1-(4-[2-{4-(4-trifluoromethylphenyl)phenoxy}ethoxy]-3-fluorophenyl)methoxy]-[4*S*,5*S*]-dimethyl-1,3,2-diazaphospholidine-2-oxide;
- 2-[1-(Bis[*N*-ethylamino]phosphoryl)-1-(4-[*N*-(2-{4-(4-trifluoromethylphenyl)phenoxy}ethyl)-*N*-methylaminocarbonyl]-3-fluorophenyl)methyl]-1,3,5,5-tetramethyl-1,3,2-diazaphosphinane-2-oxide;
- 2-[1-(Bis[*N*-ethylamino]phosphoryl)-2-(4-[3-{4-(4-trifluoromethylphenyl)phenoxy}-1-oxoprop-1-yl]-3-fluorophenyl)ethen-1-yl]-[4*S*]-ethyl-1,3,2-oxazaphospholidine-2-oxide;
- 2-[1-(Bis[*N*-ethylamino]phosphoryl)-2-(4-[2-{1-[4-(2-trifluoromethylphenyl)phenylmethyl]-3-hexylureido}ethyl]-3-fluorophenyl)eth-1-yl]-[4*R*]-methyl-1,3,2-oxazaphosphinane-2-oxide;
- 2-[2-(Bis[*N*-ethylamino]phosphoryl)-2-(4-[2-{1-butyl-3-(5-methoxypyrid-2-yl)ureido}ethyl]-3-fluorophenyl)eth-1-yl]-1,3,5,5-tetramethyl-1,3,2-diazaphosphinane-2-oxide;



- 2-[2-(Bis[*N*-ethylamino]phosphoryl)-1-(4-[3-{4-acetyl-3-hydroxy-2-propylphenoxy}propoxy]-3-fluorophenyl)eth-1-yl]-[4S]-ethyl-1,3,2-oxazaphospholidine-2-oxide;
- 2-[1-(Diethoxyphosphoryloxy)-1-(4-[2-{4*H*-3-oxobenzo[1,4]oxazin-2-yl}ethoxy]-3-fluorophenyl)methyl]-[4S,5S]-dimethyl-1,3,2-diazaphospholidine-2-oxide;
- 2-[1-(Diethoxyphosphoryl)-1-(4-[3,*N*-phthalimidopropoxy]-3-fluorophenyl)methoxy]-[4S,5S]-dimethyl-1,3,2-diazaphospholidine-2-oxide;
- 2-[1-(Diethoxyphosphoryl)-1-(4-[4,*N*-phthalimidobutoxy]-3-fluorophenyl)methyl]-1,3,5,5-tetramethyl-1,3,2-diazaphosphinane-2-oxide;
- 2-[1-(Diethoxyphosphoryl)-2-(3-[3-{*N*-methyl-*N*-pyrid-2-ylamino}propoxy]-4-fluorophenyl)ethen-1-yl]-[4S]-ethyl-1,3,2-oxazaphospholidine-2-oxide;
- 2-[1-(Diethoxyphosphoryl)-2-(3-[*N*-(3-{*N*-methyl-*N*-pyrid-2-ylamino}propyl)-*N*-methylamino]-4-fluorophenyl)eth-1-yl]-[4R]methyl-1,3,2-oxazaphosphinane-2-oxide;
- 2-[2-(Diethoxyphosphoryl)-2-(3-[3-{*N*-methyl-*N*-pyrid-2-ylamino}-1-oxoprop-1-ylamino]-4-fluorophenyl)eth-1-yl]-1,3,5,5-tetramethyl-1,3,2-diazaphosphinane-2-oxide;
- 2-[2-(Diethoxyphosphoryl)-1-(3-[3-{5-methyl-2-phenyloxazol-4-yl}propoxy]-4-fluorophenyl)eth-1-yl]-[4S]-ethyl-1,3,2-oxazaphospholidine-2-oxide;
- 2-[1-(Diethoxyphosphoryloxy)-1-(3-[*N*-(2-{5-methyl-2-phenyloxazol-4-yl}ethyl)-*N*-methylaminocarbonyl]-4-methoxyphenyl)methyl]-[4S,5S]-dimethyl-1,3,2-diazaphospholidine-2-oxide;
- 2-[1-(Diethoxyphosphoryl)-1-(3-[3-{5-methyl-2-phenylthiazol-4-yl}propoxy]-4-fluorophenyl)methoxy]-[4S,5S]-dimethyl-1,3,2-diazaphospholidine-2-oxide;

- 2-[1-(Diethoxyphosphoryl)-1-(3-[3-{5-methyl-2-phenylthiazol-4-yl}-1-oxoprop-1-yl]-4-fluorophenyl)methyl]-1,3,5,5-tetramethyl-1,3,2-diazaphosphinane-2-oxide;
- 2-[1-(Diethoxyphosphoryl)-2-(3-[4-{5-methyl-2-pyrid-4-ylloxazol-4-yl}butoxy]-4-fluorophenyl)ethen-1-yl]-[4S]-ethyl-1,3,2-oxazaphospholidine-2-oxide;
- 5 2-[1-(Diethoxyphosphoryl)-2-(3-[3-{5-methyl-2-pyrid-4-ylthiazol-4-yl}propoxy]-4-fluorophenyl)eth-1-yl]-[4R]methyl-1,3,2-oxazaphosphinane-2-oxide;
- 2-[2-(Diethoxyphosphoryl)-2-(3-[3-{5-methyl-2-pyrid-4-ylloxazol-4-yl}-1-oxoprop-1-ylthio]-4-fluorophenyl)eth-1-yl]-1,3,5,5-tetramethyl-1,3,2-diazaphosphinane-2-oxide; and
- 10 2-[2-(Diethoxyphosphoryl)-1-(3-[*N*-(3-{5-methyl-2-pyrid-4-ylthiazol-4-yl}propyl)-*N*-methylamino]-4-fluorophenyl)eth-1-yl]-[4S]-ethyl-1,3,2-oxazaphospholidine-2-oxide;

12. The pharmaceutical formulation according to Claim 7, wherein the  
15 compound of Formula I is selected from the group consisting of:

- Diethyl 1-(diethoxyphosphinyloxy)-1-(4-[2-{*N*-methyl-*N*-pyrid-2-ylamino}ethoxy]-3-fluorophenyl)methylphosphonate;
- Diethyl 1-(diethoxyphosphinyloxy)-1-(4-[3,*N*-phthalimidopropoxy]-3-fluorophenyl)methylphosphonate;
- 20 Diethyl 1-(diethoxyphosphinyloxy)-1-(4-[2-{5-methyl-2-phenyloxazol-4-yl}ethoxy]-3-fluorophenyl)methylphosphonate;
- Diethyl 1-(diethoxyphosphinyloxy)-1-(3-[3-{*N*-methyl-*N*-pyrid-2-ylamino}propoxy]-4-fluorophenyl)methylphosphonate;
- Diethyl 1-(diethoxyphosphinyloxy)-1-(3-[4-{*N*-methyl-*N*-pyrid-2-ylamino}butoxy]-4-fluorophenyl)methylphosphonate;
- 25

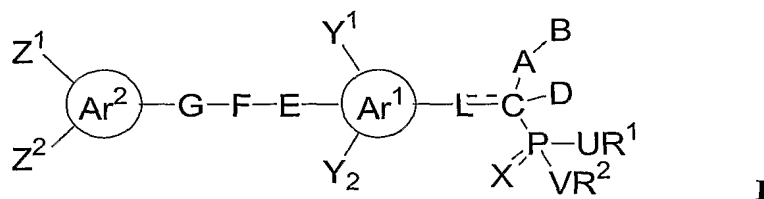
- Diethyl 1-(diethoxyphosphinyloxy)-1-(3-[4,*N*-phthalimidobutoxy]-4-fluorophenyl)methylphosphonate;
- Diethyl 1-(diethoxyphosphinyloxy)-1-(3-[5,*N*-phthalimidopentoxy]-4-fluorophenyl)methylphosphonate;
- 5 Diethyl 1-(diethoxyphosphinyloxy)-1-(3-[4-{5-methyl-2-pyrid-4-yloxazol-4-yl}butoxy]-4-fluorophenyl)methylphosphonate;
- Diethyl 1-(diethoxyphosphinyloxy)-1-(3-[5-{5-methyl-2-pyrid-4-yloxazol-4-yl}pentoxy]-4-fluorophenyl)methylphosphonate;
- 1-(4-[2-{*N*-methyl-*N*-pyrid-2-ylamino}ethoxy]-3-fluorophenyl)-1,1-bis([4*R*,5*S*]-  
 10 dimethyl-2-oxido-1,3,2-dioxaphospholan-2-yl)methane;
- 1-(4-[3,*N*-phthalimidopropoxy]-3-fluorophenyl)-1,1-bis([4*R*,5*S*]-dimethyl-2-oxido-1,3,2-dioxaphospholan-2-yl)methane;
- 1-(4-[2-{5-methyl-2-phenyloxazol-4-yl}ethoxy]-3-fluorophenyl)-1,1-bis([4*R*,5*S*]-dimethyl-2-oxido-1,3,2-dioxaphospholan-2-yl)methane;
- 15 1-(3-[3-{*N*-methyl-*N*-pyrid-2-ylamino}propoxy]-4-fluorophenyl)-1,1-bis([4*R*,5*S*]-dimethyl-2-oxido-1,3,2-dioxaphospholan-2-yl)methane;
- 1-(3-[4-{*N*-methyl-*N*-pyrid-2-ylamino}butoxy]-4-fluorophenyl)-1,1-bis([4*R*,5*S*]-dimethyl-2-oxido-1,3,2-dioxaphospholan-2-yl)methane;
- 20 1-(3-[4,*N*-phthalimidobutoxy]-4-fluorophenyl)-1,1-bis([4*R*,5*S*]-dimethyl-2-oxido-1,3,2-dioxaphospholan-2-yl)methane;
- 1-(3-[5,*N*-phthalimidopentoxy]-4-fluorophenyl)-1,1-bis([4*R*,5*S*]-dimethyl-2-oxido-1,3,2-dioxaphospholan-2-yl)methane;
- 1-(3-[4-{5-methyl-2-pyrid-4-yloxazol-4-yl}butoxy]-4-fluorophenyl)-1,1-bis([4*R*,5*S*]-dimethyl-2-oxido-1,3,2-dioxaphospholan-2-yl)methane;

- 1-(3-[5-{5-methyl-2-pyrid-4-yloxazol-4-yl}pentoxy]-4-fluorophenyl)-1,1-bis([4R,5S]-dimethyl-2-oxido-1,3,2-dioxaphospholan-2-yl)methane;
- N,N,N',N'*-Tetramethyl 1-(4-[2-{*N*-methyl-*N*-pyrid-2-ylamino}ethoxy]-3-fluorophenyl)-1-hydroxymethylphosphondiamide;
- 5 *N,N,N',N'*-Tetramethyl 1-(4-[3,*N*-phthalimidopropoxy]-3-fluorophenyl)-1-hydroxymethylphosphondiamide;
- N,N,N',N'*-Tetramethyl 1-(4-[2-{5-methyl-2-phenyloxazol-4-yl}ethoxy]-3-fluorophenyl)-1-hydroxymethylphosphondiamide;
- 2-[1-hydroxy-1-(4-[2-{*N*-methyl-*N*-pyrid-2-ylamino}ethoxy]-3-fluorophenyl)methyl]-[4S]-(1-methylethyl)-1,3,2-oxazaphospholidine-2-oxide;
- 10 2-[1-hydroxy-1-(4-[3,*N*-phthalimidopropoxy]-3-fluorophenyl)methyl]-[4S]-(1-methylethyl)-1,3,2-oxazaphospholidine-2-oxide;
- 2-[1-hydroxy-1-(4-[2-{5-methyl-2-phenyloxazol-4-yl}ethoxy]-3-fluorophenyl)methyl]-[4S]-(1-methylethyl)-1,3,2-oxazaphospholidine-2-oxide;
- 15 1-[*N*-(4-[2-{*N*-methyl-*N*-pyrid-2-ylamino}ethoxy]-3-fluorophenyl)amino]-1,1-bis(bis[*N*-ethylamino]phosphoryl)methane;
- 1-[*N*-(4-[3,*N*-phthalimidopropoxy]-3-fluorophenyl)amino]-1,1-bis(bis[*N*-ethylamino]phosphoryl)methane; and
- 1-[*N*-(4-[2-{5-methyl-2-phenyloxazol-4-yl}ethoxy]-3-fluorophenyl)amino]-1,1-bis(bis[*N*-ethylamino]phosphoryl)methane.
- 20

13. A pharmaceutical formulation according to Claim 7, wherein the pharmaceutically acceptable carrier, excipient, solvent, adjuvant or diluent is selected from the group consisting of edible carriers, gelatin, gum tragacanth, acacia, corn starch,
- 25 gelatin, microcrystalline cellulose, starch, lactose, alginic acid, magnesium stearate,

colloidal silicon dioxide, sucrose, saccharin, peppermint, methyl salicylate, fruit  
 flavoring, a fatty oil, a syrup, a preservative, a dye, coloring, a sterile diluent such as  
 water for injection, saline solution, fixed oil, a naturally occurring vegetable oil, sesame  
 oil, coconut oil, peanut oil, cottonseed oil, a synthetic fatty oil, ethyl oleate, polyethylene  
 glycol, glycerine, propylene glycol, a synthetic solvent, an antimicrobial agent, benzyl  
 alcohol, methyl parabens, an antioxidant, ascorbic acid, sodium bisulfite, a chelating  
 agent, ethylenediaminetetraacetic acid (EDTA), a buffers, an acetates, a citratee, a  
 phosphate, an agent for the adjustment of tonicity, sodium chloride, dextrose, physiological  
 saline, phosphate buffered saline (PBS), a thickener, a solubilizer, glucose, polyethylene  
 glycol, polypropyleneglycol and iposomal suspensions including tissue-targeted  
 liposomes.

14. A method of regulating HDL and LDL cholesterol levels in a mammal  
 comprising administering to a mammal an effective amount of a compound of the  
 formula (I):



wherein

- A is a bond, O, CH<sub>2</sub>, CHF, CF<sub>2</sub>, or NR<sub>6</sub>;
- B is H, C<sub>1</sub>-C<sub>6</sub> lower alkyl, or P(=X<sup>1</sup>)(UR<sup>3</sup>)(VR<sup>4</sup>);
- D is a) H or lower alkyl, wherein the L=C bond is a single bond; or  
 b) OH, OCOR<sup>5</sup>, NH<sub>2</sub>, NR<sup>6</sup>R<sup>6a</sup>, or NHCOR<sup>5</sup>, wherein the L=C bond is a single  
 bond, with the proviso that A is CH<sub>2</sub>, CHF, CF<sub>2</sub>;

L is a)  $\text{NR}^6$ ,  $\text{CR}^7\text{R}^8$ ,  $-\text{OCR}^7\text{R}^8-$ ,  $-\text{NR}^6\text{CR}^7\text{R}^8-$ , or  $-\text{S}(\text{O})_m\text{CR}^7\text{R}^8-$ , wherein the  $\text{L}=\text{C}$  bond is a single bond; or

b)  $\text{CR}^7$ , wherein the  $\text{L}=\text{C}$  bond is a double bond, with the proviso that D is absent when the  $\text{L}=\text{C}$  bond is a double bond; or

5 c) absent, wherein C is covalently bonded by a single bond to  $\text{Ar}^1$ ;

$\text{Ar}^1$  and  $\text{Ar}^2$  are each independently mono- or bicyclic aromatic rings of 5-12 atoms, including, but not limited to phenyl, pyridyl, pyrimidyl, pyrazinyl, pyridazinyl, thienyl, furanyl, pyrrolyl, imidazyl, pyrazolyl, oxazolyl, isoxazolyl, thiazolyl, isothiazolyl, 1,3,4-oxadiazolyl, 1,2,4-oxadiazolyl, 1,3,4-thiadiazolyl, 1,2,3-  
10 triazolyl, 1,3,4-triazolyl, 1,2,4-triazinyl, 1,3,5-triazinyl, benzofuranyl, benzothienyl, indolyl, indazolyl, benzimidazyl, benzoxazolyl, benzoisoxazolyl, benzothiazolyl, benzoisothiazolyl, quinoliny, isoquinoliny, quinazoliny, quinoxaliny, naphthyridyl, or puriny;

$\text{Y}^1$ ,  $\text{Y}^2$ , and  $\text{Z}^1$  are each independently a lone electron pair, H,  $\text{C}_1$ - $\text{C}_6$  lower alkyl,  $\text{C}_2$ -  
15  $\text{C}_6$  lower alkenyl,  $\text{C}_2$ - $\text{C}_6$  lower alkynyl,  $\text{C}_1$ - $\text{C}_6$  lower alkoxy,  $\text{C}_1$ - $\text{C}_6$  lower alkylamino,  $\text{C}_1$ - $\text{C}_6$  lower dialkylamino,  $\text{C}_2$ - $\text{C}_6$  lower cycloalkyl,  $\text{C}_4$ - $\text{C}_6$  lower cycloalkenyl,  $\text{C}_1$ - $\text{C}_6$  lower thioalkyl,  $\text{C}_1$ - $\text{C}_6$  lower sulfinylalkyl,  $\text{C}_1$ - $\text{C}_6$  lower sulfonylalkyl,  $\text{C}_1$ - $\text{C}_6$  lower acyloxy,  $\text{C}_1$ - $\text{C}_6$  lower acylamino with N substituted with  $\text{R}^6$ ,  $\text{CH}_2\text{OR}^5$ ,  $\text{CH}_2\text{NR}^6\text{R}^{6a}$ ,  $\text{R}_f$ ,  $\text{R}_f\text{O}$ , OH,  $\text{NH}_2$ , CN,  $\text{NO}_2$ , F, Cl, Br, I, or  $\text{N}_3$ ;

20 E is a bond,  $\text{S}(\text{O})_m$ ,  $\text{NR}^6$ ,  $\text{C}=\text{O}$ ,  $\text{CO}_2$ ,  $\text{CONR}^6$ , O,  $-\text{OC}=\text{O}$ ,  $\text{NR}^6\text{C}=\text{O}$ ,  $\text{NR}^6\text{CO}_2$ ,  $\text{OC}=\text{ONR}^6$ ,  $\text{OCO}_2$ , or  $\text{NR}^6\text{CONR}^{6a}$ ;

F is  $(\text{CH}_2)_n$ ,  $(\text{CH}_2)_o\text{O}(\text{CH}_2)_p$ ,  $(\text{CH}_2)_o\text{NR}^6(\text{CH}_2)_p$ ,  $(\text{CH}_2)_o\text{NR}^6\text{CO}(\text{CH}_2)_p$ ,  $(\text{CH}_2)_o\text{CONR}^6$   
 $(\text{CH}_2)_p$ ,  $(\text{CH}_2)_o(\text{CR}^6=\text{CR}^6)_q(\text{CH}_2)_p$ ,  $(\text{CH}_2)_o-(\text{C}\equiv\text{C})_q-(\text{CH}_2)_p$ ;

G is a bond, O,  $\text{NR}^6$ , CO,  $\text{CO}_2$ , OCO,  $\text{OCO}_2$ ,  $\text{S}(\text{O})_m$ ,  $\text{CONR}^6$ ,  $\text{NR}^6\text{CO}$ ,  $\text{NR}^6\text{CO}_2$ ,  
25  $\text{OCONR}^6$ ,  $\text{NR}^6\text{CONR}^{6a}$ , or G can optionally be attached to  $\text{Ar}^2$  at two contiguous

C atoms to form a 5- to 7-membered partially saturated ring, which contains 0, 1, or 2 heteroatoms selected from the group consisting of O, N, and S;

X, X<sup>1</sup> are independently O or S

Z<sup>2</sup> is nothing, H or Ar<sup>1</sup> optionally substituted with Y<sup>1</sup> and Y<sup>2</sup>;

5 R<sup>1</sup>, R<sup>2</sup>, R<sup>3</sup>, and R<sup>4</sup>, are each independently selected from H, C<sub>1</sub>-C<sub>6</sub> lower alkyl, C<sub>3</sub>-C<sub>6</sub> lower alkenyl, C<sub>3</sub>-C<sub>6</sub> lower alkynyl, C<sub>3</sub>-C<sub>6</sub> lower cycloalkyl, C<sub>4</sub>-C<sub>6</sub> lower cycloalkenyl, or independently R<sup>1</sup> and R<sup>2</sup> or R<sup>3</sup> and R<sup>4</sup> can be taken together to form a 5 to 8-membered ring containing 2-7 carbon atoms, the 5 to 8-membered ring optionally substituted with zero to 3 substituents selected from the group C<sub>1</sub>-  
10 C<sub>4</sub> lower alkyl, C<sub>1</sub>-C<sub>4</sub> lower alkoxy, C<sub>1</sub>-C<sub>4</sub> lower alkylamino, C<sub>1</sub>-C<sub>4</sub> lower dialkylamino, amino, hydroxyl, hydroxymethyl, methoxymethyl, phenyl, substituted phenyl, benzyl, substituted benzyl;

U and V are each independently a bond, O or NR<sup>6</sup>;

15 R<sup>5</sup> R<sup>6</sup> and R<sup>6a</sup> are each independently C<sub>1</sub>-C<sub>6</sub> alkyl, C<sub>3</sub>-C<sub>6</sub> cycloalkyl, C<sub>3</sub>-C<sub>6</sub> alkenyl, C<sub>3</sub>-C<sub>6</sub> cycloalkenyl, C<sub>3</sub>-C<sub>6</sub> alkynyl, and H;

R<sup>7</sup> and R<sup>8</sup> are each independently H, C<sub>1</sub>-C<sub>4</sub> lower alkyl, or are taken together to form a saturated C<sub>3</sub>-C<sub>6</sub> carbocyclic ring;

R<sub>f</sub> is C<sub>1</sub>-C<sub>4</sub> straight or branched lower perfluoroalkyl;

all lower alkyl, alkenyl and alkynyl groups including those linked via heteroatoms can  
20 be straight chain or branched;

m is 0, 1, or 2;

n is 0, 1, 2, 3, 4, 5, or 6;

o is 0, 1, 2, 3, 4, 5, or 6;

p is 0, 1, 2, 3, 4, 5, or 6; and

25 q is 0, 1, 2, 3, 4, 5, or 6;

with the provisos that

when A is a bond or O, B is  $P(O)(OR^3)(OR^4)$ , and D is selected from the group H, OH,  $OCOCH_3$ , and  $NH_2$ , and when  $R^1 = R^2$  and  $R^3 = R^4$ , and both are selected from the group H or unsubstituted  $C_1$ - $C_4$  lower alkyl, and E and G are bonds, and F is  
 5  $(CH_2)_n$  where n is 0, and both  $Ar^1$  and  $Ar^2$  are phenyl, then at least one of  $Y^1$ ,  $Y^2$ ,  $Z^1$ , or  $Z^2$  must not be H; and

when A is a bond or  $CH_2$ , and B is  $P(O)(OR^3)(OR^4)$ , and either D is H or  $C_1$ - $C_4$  lower alkyl where L is  $CH_2$ , or D is absent, with  $L-C$  taken together represent an ethenylidene group, and  $Ar^1$  is phenyl, and E is a bond or O, and  $R^1 = R^2$  and  $R^3 = R^4$ ,  
 10 and both are drawn from the group H or  $C_1$ - $C_6$  unsubstituted lower alkyl, then one of  $Y^1$  and  $Y^2$  must be other than H or unsubstituted  $C_1$ - $C_4$  lower alkyl or unsubstituted  $C_1$ - $C_4$  lower alkoxy; and

when A is O, and B is H or  $P(O)(OR^3)(OR^4)$ , and  $R^1$ ,  $R^2$ ,  $R^3$ , and  $R^4$  are all selected from the group H or  $C_1$ - $C_6$  unsubstituted lower alkyl, and D is H, and L is a  
 15 bond, and  $Ar^1$  is phenyl, and E is other than a bond or O, then one of  $Y^1$  or  $Y^2$  must be other than H, or  $C_1$ - $C_4$  unsubstituted lower alkyl or  $C_1$ - $C_4$  unsubstituted lower alkoxy;

or a pharmaceutically acceptable salt thereof.

20 15. A method according to claim 14, wherein the mammal is a human.

16. A method according to claim 14, wherein the effective amount is administered in a dosage of between about 0.1 mg to about 5000 mg per day.

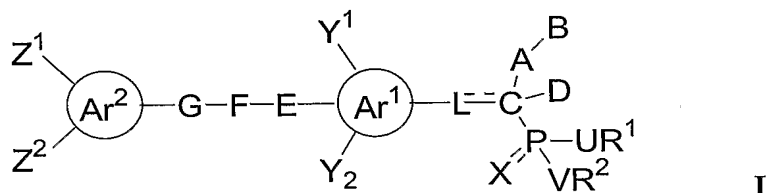


17. A method according to claim 14, wherein the effective amount is administered in a dosage of between about 50 mg to about 500 mg per day.

18. A method according to claim 14, wherein the effective amount of the pharmaceutical formulation is administered orally.

19. A method according to claim 14, wherein the effective amount of the pharmaceutical formulation is administered by depot injection.

20. A method of regulating HDL or LDL cholesterol levels in a mammal comprising administering to a mammal an effective amount of a pharmaceutical formulation comprising a compound of the formula (I):



wherein

A is a bond, O, CH<sub>2</sub>, CHF, CF<sub>2</sub>, or NR<sub>6</sub>;

B is H, C<sub>1</sub>-C<sub>6</sub> lower alkyl, or P(=X<sup>1</sup>)(UR<sup>3</sup>)(VR<sup>4</sup>);

D is a) H or lower alkyl, wherein the L=C bond is a single bond; or

b) OH, OCOR<sup>5</sup>, NH<sub>2</sub>, NR<sup>6</sup>R<sup>6a</sup>, or NHCOR<sup>5</sup>, wherein the L=C bond is a single bond, with the proviso that A is CH<sub>2</sub>, CHF, CF<sub>2</sub>;

L is a) NR<sup>6</sup>, CR<sup>7</sup>R<sup>8</sup>, -OCR<sup>7</sup>R<sup>8</sup>-, -NR<sup>6</sup>CR<sup>7</sup>R<sup>8</sup>-, or -S(O)<sub>m</sub>CR<sup>7</sup>R<sup>8</sup>-, wherein the L=C bond is a single bond; or

b)  $CR^7$ , wherein the  $L \equiv C$  bond is a double bond, with the proviso that D is absent when the  $L \equiv C$  bond is a double bond; or

c) absent, wherein C is covalently bonded by a single bond to  $Ar^1$ ;

$Ar^1$  and  $Ar^2$  are each independently mono- or bicyclic aromatic rings of 5-12 atoms, including, but not limited to phenyl, pyridyl, pyrimidyl, pyrazinyl, pyridazinyl, thienyl, furanyl, pyrrolyl, imidazolyl, pyrazolyl, oxazolyl, isoxazolyl, thiazolyl, isothiazolyl, 1,3,4-oxadiazolyl, 1,2,4-oxadiazolyl, 1,3,4-thiadiazolyl, 1,2,3-triazolyl, 1,3,4-triazolyl, 1,2,4-triazinyl, 1,3,5-triazinyl, benzofuranyl, benzothienyl, indolyl, indazolyl, benzimidazolyl, benzoxazolyl, benzoisoxazolyl, benzothiazolyl, benzoisothiazolyl, quinolinyl, isoquinolinyl, quinazolinyl, quinoxalinyl, naphthyridyl, or purinyl;

$Y^1$ ,  $Y^2$ , and  $Z^1$  are each independently a lone electron pair, H,  $C_1$ - $C_6$  lower alkyl,  $C_2$ - $C_6$  lower alkenyl,  $C_2$ - $C_6$  lower alkynyl,  $C_1$ - $C_6$  lower alkoxy,  $C_1$ - $C_6$  lower alkylamino,  $C_1$ - $C_6$  lower dialkylamino,  $C_2$ - $C_6$  lower cycloalkyl,  $C_4$ - $C_6$  lower cycloalkenyl,  $C_1$ - $C_6$  lower thioalkyl,  $C_1$ - $C_6$  lower sulfinylalkyl,  $C_1$ - $C_6$  lower sulfonylalkyl,  $C_1$ - $C_6$  lower acyloxy,  $C_1$ - $C_6$  lower acylamino with N substituted with  $R^6$ ,  $CH_2OR^5$ ,  $CH_2NR^6R^{6a}$ ,  $R^6$ ,  $R^6O$ , OH,  $NH_2$ , CN,  $NO_2$ , F, Cl, Br, I, or  $N_3$ ;

E is a bond,  $S(O)_m$ ,  $NR^6$ ,  $C=O$ ,  $CO_2$ ,  $CONR^6$ , O,  $-OC=O$ ,  $NR^6C=O$ ,  $NR^6CO_2$ ,  $OC=ONR^6$ ,  $OCO_2$ , or  $NR^6CONR^{6a}$ ;

F is  $(CH_2)_n$ ,  $(CH_2)_oO(CH_2)_p$ ,  $(CH_2)_oNR^6(CH_2)_p$ ,  $(CH_2)_oNR^6CO(CH_2)_p$ ,  $(CH_2)_oCONR^6(CH_2)_p$ ,  $(CH_2)_o(CR^6=CR^6)(CH_2)_p$ ,  $(CH_2)_o-(C \equiv C)_q-(CH_2)_p$ ;

G is a bond, O,  $NR^6$ , CO,  $CO_2$ , OCO,  $OCO_2$ ,  $S(O)_m$ ,  $CONR^6$ ,  $NR^6CO$ ,  $NR^6CO_2$ ,  $CONR^6$ ,  $NR^6CONR^{6a}$ , or G can optionally be attached to  $Ar^2$  at two contiguous C atoms to form a 5- to 7-membered partially saturated ring, which contains 0, 1, or 2 heteroatoms selected from the group consisting of O, N, and S;

- X, X<sup>1</sup> are independently O or S
- Z<sup>2</sup> is nothing, H or Ar<sup>1</sup> optionally substituted with Y<sup>1</sup> and Y<sup>2</sup>;
- R<sup>1</sup>, R<sup>2</sup>, R<sup>3</sup>, and R<sup>4</sup>, are each independently selected from H, C<sub>1</sub>-C<sub>6</sub> lower alkyl, C<sub>3</sub>-C<sub>6</sub> lower alkenyl, C<sub>3</sub>-C<sub>6</sub> lower alkynyl, C<sub>3</sub>-C<sub>6</sub> lower cycloalkyl, C<sub>4</sub>-C<sub>6</sub> lower cycloalkenyl, or independently R<sup>1</sup> and R<sup>2</sup> or R<sup>3</sup> and R<sup>4</sup> can be taken together to form a 5 to 8-membered ring containing 2-7 carbon atoms, the 5 to 8-membered ring optionally substituted with zero to 3 substituents selected from the group C<sub>1</sub>-C<sub>4</sub> lower alkyl, C<sub>1</sub>-C<sub>4</sub> lower alkoxy, C<sub>1</sub>-C<sub>4</sub> lower alkylamino, C<sub>1</sub>-C<sub>4</sub> lower dialkylamino, amino, hydroxyl, hydroxymethyl, methoxymethyl, phenyl, substituted phenyl, benzyl, substituted benzyl;
- U and V are each independently a bond, O or NR<sup>6</sup>;
- R<sup>5</sup> R<sup>6</sup> and R<sup>6a</sup> are each independently C<sub>1</sub>-C<sub>6</sub> alkyl, C<sub>3</sub>-C<sub>6</sub> cycloalkyl, C<sub>3</sub>-C<sub>6</sub> alkenyl, C<sub>3</sub>-C<sub>6</sub> cycloalkenyl, C<sub>3</sub>-C<sub>6</sub> alkynyl, and H;
- R<sup>7</sup> and R<sup>8</sup> are each independently H, C<sub>1</sub>-C<sub>4</sub> lower alkyl, or are taken together to form a saturated C<sub>3</sub>-C<sub>6</sub> carbocyclic ring;
- R<sub>f</sub> is C<sub>1</sub>-C<sub>4</sub> straight or branched lower perfluoroalkyl;
- all lower alkyl, alkenyl and alkynyl groups including those linked via heteroatoms can be straight chain or branched;
- m is 0, 1, or 2;
- n is 0, 1, 2, 3, 4, 5, or 6;
- o is 0, 1, 2, 3, 4, 5, or 6;
- p is 0, 1, 2, 3, 4, 5, or 6; and
- q is 0, 1, 2, 3, 4, 5, or 6;
- with the provisos that

when A is a bond or O, B is  $P(O)(OR^3)(OR^4)$ , and D is selected from the group H, OH,  $OCOCH_3$ , and  $NH_2$ , and when  $R^1 = R^2$  and  $R^3 = R^4$ , and both are selected from the group H or unsubstituted  $C_1$ - $C_4$  lower alkyl, and E and G are bonds, and F is  $(CH_2)_n$  where n is 0, and both  $Ar^1$  and  $Ar^2$  are phenyl, then at least one of  $Y^1$ ,  $Y^2$ ,  $Z^1$ , or  $Z^2$  must not be H; and

when A is a bond or  $CH_2$ , and B is  $P(O)(OR^3)(OR^4)$ , and either D is H or  $C_1$ - $C_4$  lower alkyl where L is  $CH_2$ , or D is absent, with  $L \equiv C$  taken together represent an ethenylidene group, and  $Ar^1$  is phenyl, and E is a bond or O, and  $R^1 = R^2$  and  $R^3 = R^4$ , and both are drawn from the group H or  $C_1$ - $C_6$  unsubstituted lower alkyl, then one of  $Y^1$  and  $Y^2$  must be other than H or unsubstituted  $C_1$ - $C_4$  lower alkyl or unsubstituted  $C_1$ - $C_4$  lower alkoxy; and

when A is O, and B is H or  $P(O)(OR^3)(OR^4)$ , and  $R^1$ ,  $R^2$ ,  $R^3$ , and  $R^4$  are all selected from the group H or  $C_1$ - $C_6$  unsubstituted lower alkyl, and D is H, and L is a bond, and  $Ar^1$  is phenyl, and E is other than a bond or O, then one of  $Y^1$  or  $Y^2$  must be other than H, or  $C_1$ - $C_4$  unsubstituted lower alkyl or  $C_1$ - $C_4$  unsubstituted lower alkoxy;

or a pharmaceutically acceptable salt thereof;

and a pharmaceutically acceptable carrier, excipient, solvent, adjuvant or diluent.

21. A method according to claim 20, wherein the mammal is a human.

22. A method according to claim 20, wherein the effective amount is administered in a dosage of between about 0.1 mg to about 5000 mg per day.

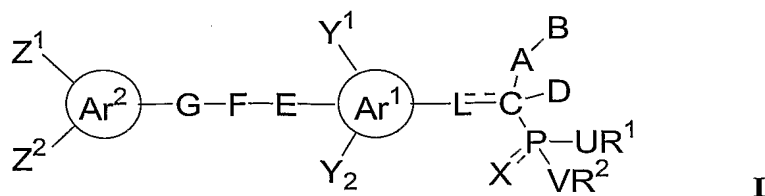
23. A method according to claim 22, wherein the effective amount comprises a dosage of between about 50 mg to about 500 mg per day.

24. A method according to claim 20, wherein the effective amount of the pharmaceutical formulation is administered orally.

25. A method according to claim 20, wherein the effective amount of the pharmaceutical formulation is administered depot injection.

26. A method according to claim 20, wherein the pharmaceutically acceptable carrier, excipient, solvent, adjuvant or diluent is selected from the group consisting of edible carriers, gelatin, gum tragacanth, acacia, corn starch, gelatin, microcrystalline cellulose, starch, lactose, alginic acid, magnesium stearate, colloidal silicon dioxide, sucrose, saccharin, peppermint, methyl salicylate, fruit flavoring, a fatty oil, a syrup, a preservative, a dye, coloring, a sterile diluent such as water for injection, saline solution, fixed oil, a naturally occurring vegetable oil, sesame oil, coconut oil, peanut oil, cottonseed oil, a synthetic fatty oil, ethyl oleate, polyethylene glycol, glycerine, propylene glycol, a synthetic solvent, an antimicrobial agent, benzyl alcohol, methyl parabens, an antioxidantm, ascorbic acid, sodium bisulfite, a chelating agent, ethylenediaminetetraacetic acid (EDTA), a buffers, an acetates, a citratee, a phosphate, an agent for the adjustment of tonicity, sodium chloride, dextrose, pysiological saline, phosphate buffered saline (PBS), a thickener, a solubilizer, glucose, polyethylene glycol, polypropyleneglycol and iposomal suspensions including tissue-targeted liposomes.

27. A method of treating disease states related to HDL or LDL cholesterol levels comprising administering to a mammal in need of such treatment a therapeutically effective amount of a compound of the formula (I):



5 wherein

A is a bond, O, CH<sub>2</sub>, CHF, CF<sub>2</sub>, or NR<sub>6</sub>;

B is H, C<sub>1</sub>-C<sub>6</sub> lower alkyl, or P(=X<sup>1</sup>)(UR<sup>3</sup>)(VR<sup>4</sup>);

D is a) H or lower alkyl, wherein the L=C bond is a single bond; or

b) OH, OCOR<sup>5</sup>, NH<sub>2</sub>, NR<sup>6</sup>R<sup>6a</sup>, or NHCOR<sup>5</sup>, wherein the L=C bond is a single bond, with the proviso that A is CH<sub>2</sub>, CHF, CF<sub>2</sub>;

L is a) NR<sup>6</sup>, CR<sup>7</sup>R<sup>8</sup>, -OCR<sup>7</sup>R<sup>8</sup>-, -NR<sup>6</sup>CR<sup>7</sup>R<sup>8</sup>-, or -S(O)<sub>m</sub>CR<sup>7</sup>R<sup>8</sup>-, wherein the L=C bond is a single bond; or

b) CR<sup>7</sup>, wherein the L=C bond is a double bond, with the proviso that D is absent when the L=C bond is a double bond; or

c) absent, wherein C is covalently bonded by a single bond to Ar<sup>1</sup>;

Ar<sup>1</sup> and Ar<sup>2</sup> are each independently mono- or bicyclic aromatic rings of 5-12 atoms, including, but not limited to phenyl, pyridyl, pyrimidyl, pyrazinyl, pyridazinyl, thienyl, furanyl, pyrrolyl, imidazyl, pyrazolyl, oxazolyl, isoxazolyl, thiazolyl, isothiazolyl, 1,3,4-oxadiazolyl, 1,2,4-oxadiazolyl, 1,3,4-thiadiazolyl, 1,2,3-triazolyl, 1,3,4-triazolyl, 1,2,4-triazinyl, 1,3,5-triazinyl, benzofuranyl, benzothienyl, indolyl, indazolyl, benzimidazyl, benzoxazolyl, benzoisoxazolyl,

benzothiazoyl, benzoisothiazolyl, quinoliny, isoquinoliny, quinazoliny, quinoxaliny, naphthyridyl, or puriny;

$Y^1$ ,  $Y^2$ , and  $Z^1$  are each independently a lone electron pair, H, C<sub>1</sub>-C<sub>6</sub> lower alkyl, C<sub>2</sub>-C<sub>6</sub> lower alkenyl, C<sub>2</sub>-C<sub>6</sub> lower alkynyl, C<sub>1</sub>-C<sub>6</sub> lower alkoxy, C<sub>1</sub>-C<sub>6</sub> lower alkylamino, C<sub>1</sub>-C<sub>6</sub> lower dialkylamino, C<sub>2</sub>-C<sub>6</sub> lower cycloalkyl, C<sub>4</sub>-C<sub>6</sub> lower cycloalkenyl, C<sub>1</sub>-C<sub>6</sub> lower thioalkyl, C<sub>1</sub>-C<sub>6</sub> lower sulfinylalkyl, C<sub>1</sub>-C<sub>6</sub> lower sulfonylalkyl, C<sub>1</sub>-C<sub>6</sub> lower acyloxy, C<sub>1</sub>-C<sub>6</sub> lower acylamino with N substituted with R<sup>6</sup>, CH<sub>2</sub>OR<sup>5</sup>, CH<sub>2</sub>NR<sup>6</sup>R<sup>6a</sup>, R<sub>f</sub>, R<sub>f</sub>O, OH, NH<sub>2</sub>, CN, NO<sub>2</sub>, F, Cl, Br, I, or N<sub>3</sub>;

E is a bond, S(O)<sub>m</sub>, NR<sup>6</sup>, C=O, CO<sub>2</sub>, CONR<sup>6</sup>, O, -OC=O, NR<sup>6</sup>C=O, NR<sup>6</sup>CO<sub>2</sub>, OC=ONR<sup>6</sup>, OCO<sub>2</sub>, or NR<sup>6</sup>CONR<sup>6a</sup>;

F is (CH<sub>2</sub>)<sub>n</sub>, (CH<sub>2</sub>)<sub>o</sub>O(CH<sub>2</sub>)<sub>p</sub>, (CH<sub>2</sub>)<sub>o</sub>NR<sup>6</sup>(CH<sub>2</sub>)<sub>p</sub>, (CH<sub>2</sub>)<sub>o</sub>NR<sup>6</sup>CO(CH<sub>2</sub>)<sub>p</sub>, (CH<sub>2</sub>)<sub>o</sub>CONR<sup>6</sup>(CH<sub>2</sub>)<sub>p</sub>, (CH<sub>2</sub>)<sub>o</sub>(CR<sup>6</sup>=CR<sup>6</sup>)<sub>q</sub>(CH<sub>2</sub>)<sub>p</sub>, (CH<sub>2</sub>)<sub>o</sub>-(C≡C)<sub>q</sub>-(CH<sub>2</sub>)<sub>p</sub>;

G is a bond, O, NR<sup>6</sup>, CO, CO<sub>2</sub>, OCO, OCO<sub>2</sub>, S(O)<sub>m</sub>, CONR<sup>6</sup>, NR<sup>6</sup>CO, NR<sup>6</sup>CO<sub>2</sub>, OCONR<sup>6</sup>, NR<sup>6</sup>CONR<sup>6a</sup>, or G can optionally be attached to Ar<sup>2</sup> at two contiguous

C atoms to form a 5- to 7-membered partially saturated ring, which contains 0, 1, or 2 heteroatoms selected from the group consisting of O, N, and S;

X, X<sup>1</sup> are independently O or S

Z<sup>2</sup> is nothing, H or Ar<sup>1</sup> optionally substituted with Y<sup>1</sup> and Y<sup>2</sup>;

R<sup>1</sup>, R<sup>2</sup>, R<sup>3</sup>, and R<sup>4</sup>, are each independently selected from H, C<sub>1</sub>-C<sub>6</sub> lower alkyl, C<sub>3</sub>-C<sub>6</sub> lower alkenyl, C<sub>3</sub>-C<sub>6</sub> lower alkynyl, C<sub>3</sub>-C<sub>6</sub> lower cycloalkyl, C<sub>4</sub>-C<sub>6</sub> lower cycloalkenyl, or independently R<sup>1</sup> and R<sup>2</sup> or R<sup>3</sup> and R<sup>4</sup> can be taken together to form a 5 to 8-membered ring containing 2-7 carbon atoms, the 5 to 8-membered ring optionally substituted with zero to 3 substituents selected from the group C<sub>1</sub>-C<sub>4</sub> lower alkyl, C<sub>1</sub>-C<sub>4</sub> lower alkoxy, C<sub>1</sub>-C<sub>4</sub> lower alkylamino, C<sub>1</sub>-C<sub>4</sub> lower

dialkylamino, amino, hydroxyl, hydroxymethyl, methoxymethyl, phenyl, substituted phenyl, benzyl, substituted benzyl;

U and V are each independently a bond, O or  $\text{NR}^6$ ;

$\text{R}^5$ ,  $\text{R}^6$  and  $\text{R}^{6a}$  are each independently  $\text{C}_1$ - $\text{C}_6$  alkyl,  $\text{C}_3$ - $\text{C}_6$  cycloalkyl,  $\text{C}_3$ - $\text{C}_6$  alkenyl,  $\text{C}_3$ - $\text{C}_6$  cycloalkenyl,  $\text{C}_3$ - $\text{C}_6$  alkynyl, and H;

$\text{R}^7$  and  $\text{R}^8$  are each independently H,  $\text{C}_1$ - $\text{C}_4$  lower alkyl, or are taken together to form a saturated  $\text{C}_3$ - $\text{C}_6$  carbocyclic ring;

$\text{R}_f$  is  $\text{C}_1$ - $\text{C}_4$  straight or branched lower perfluoroalkyl;

all lower alkyl, alkenyl and alkynyl groups including those linked via heteroatoms can be straight chain or branched;

m is 0, 1, or 2;

n is 0, 1, 2, 3, 4, 5, or 6;

o is 0, 1, 2, 3, 4, 5, or 6;

p is 0, 1, 2, 3, 4, 5, or 6; and

q is 0, 1, 2, 3, 4, 5, or 6;

with the provisos that

when A is a bond or O, B is  $\text{P}(\text{O})(\text{OR}^3)(\text{OR}^4)$ , and D is selected from the group H, OH,  $\text{OCOCH}_3$ , and  $\text{NH}_2$ , and when  $\text{R}^1 = \text{R}^2$  and  $\text{R}^3 = \text{R}^4$ , and both are selected from the group H or unsubstituted  $\text{C}_1$ - $\text{C}_4$  lower alkyl, and E and G are bonds, and F is  $(\text{CH}_2)_n$  where n is 0, and both  $\text{Ar}^1$  and  $\text{Ar}^2$  are phenyl, then at least one of  $\text{Y}^1$ ,  $\text{Y}^2$ ,  $\text{Z}^1$ , or  $\text{Z}^2$  must not be H; and

when A is a bond or  $\text{CH}_2$ , and B is  $\text{P}(\text{O})(\text{OR}^3)(\text{OR}^4)$ , and either D is H or  $\text{C}_1$ - $\text{C}_4$  lower alkyl where L is  $\text{CH}_2$ , or D is absent, with  $\text{L}=\text{C}$  taken together represent an ethenylidene group, and  $\text{Ar}^1$  is phenyl, and E is a bond or O, and  $\text{R}^1 = \text{R}^2$  and  $\text{R}^3 = \text{R}^4$ , and both are drawn from the group H or  $\text{C}_1$ - $\text{C}_6$  unsubstituted lower alkyl, then one of

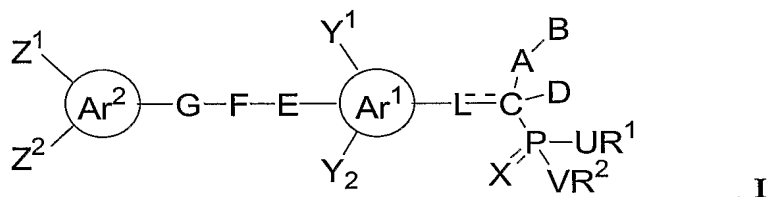


$Y^1$  and  $Y^2$  must be other than H or unsubstituted  $C_1$ - $C_4$  lower alkyl or unsubstituted  $C_1$ - $C_4$  lower alkoxy; and

when A is O, and B is H or  $P(O)(OR^3)(OR^4)$ , and  $R^1$ ,  $R^2$ ,  $R^3$ , and  $R^4$  are all selected from the group H or  $C_1$ - $C_6$  unsubstituted lower alkyl, and D is H, and L is a bond, and  $Ar^1$  is phenyl, and E is other than a bond or O, then one of  $Y^1$  or  $Y^2$  must be other than H, or  $C_1$ - $C_4$  unsubstituted lower alkyl or  $C_1$ - $C_4$  unsubstituted lower alkoxy;

or a pharmaceutically acceptable salt thereof.

28. A method of treating disease states related to HDL or LDL cholesterol levels comprising administering to a mammal in need of such treatment a combination of a therapeutically effective amount of a compound of the formula (I):



wherein

A is a bond, O,  $CH_2$ , CHF,  $CF_2$ , or  $NR_6$ ;

B is H,  $C_1$ - $C_6$  lower alkyl, or  $P(=X^1)(UR^3)(VR^4)$ ;

D is a) H or lower alkyl, wherein the  $L=C$  bond is a single bond; or

b) OH,  $OCOR^5$ ,  $NH_2$ ,  $NR^6R^{6a}$ , or  $NHCOR^5$ , wherein the  $L=C$  bond is a single bond, with the proviso that A is  $CH_2$ , CHF,  $CF_2$ ;

L is a)  $NR^6$ ,  $CR^7R^8$ ,  $-OCR^7R^8-$ ,  $-NR^6CR^7R^8-$ , or  $-S(O)_mCR^7R^8-$ , wherein the  $L=C$  bond is a single bond; or

b)  $\text{CR}^7$ , wherein the  $\text{L}\equiv\text{C}$  bond is a double bond, with the proviso that D is absent when the  $\text{L}\equiv\text{C}$  bond is a double bond; or

c) absent, wherein C is covalently bonded by a single bond to  $\text{Ar}^1$ ;

$\text{Ar}^1$  and  $\text{Ar}^2$  are each independently mono- or bicyclic aromatic rings of 5-12 atoms,

5 including, but not limited to phenyl, pyridyl, pyrimidyl, pyrazinyl, pyridazinyl, thienyl, furanyl, pyrrolyl, imidazolyl, pyrazolyl, oxazolyl, isoxazolyl, thiazolyl, isothiazolyl, 1,3,4-oxadiazolyl, 1,2,4-oxadiazolyl, 1,3,4-thiadiazolyl, 1,2,3-triazolyl, 1,3,4-triazolyl, 1,2,4-triazinyl, 1,3,5-triazinyl, benzofuranyl, benzothienyl, indolyl, indazolyl, benzimidazolyl, benzoxazolyl, benzoisoxazolyl, 10 benzothiazolyl, benzoisothiazolyl, quinolinyl, isoquinolinyl, quinazolinyl, quinoxalinyl, naphthyridyl, or purinyl;

$\text{Y}^1$ ,  $\text{Y}^2$ , and  $\text{Z}^1$  are each independently a lone electron pair, H,  $\text{C}_1\text{-C}_6$  lower alkyl,  $\text{C}_2\text{-C}_6$  lower alkenyl,  $\text{C}_2\text{-C}_6$  lower alkynyl,  $\text{C}_1\text{-C}_6$  lower alkoxy,  $\text{C}_1\text{-C}_6$  lower alkylamino,  $\text{C}_1\text{-C}_6$  lower dialkylamino,  $\text{C}_2\text{-C}_6$  lower cycloalkyl,  $\text{C}_4\text{-C}_6$  lower 15 cycloalkenyl,  $\text{C}_1\text{-C}_6$  lower thioalkyl,  $\text{C}_1\text{-C}_6$  lower sulfinylalkyl,  $\text{C}_1\text{-C}_6$  lower sulfonylalkyl,  $\text{C}_1\text{-C}_6$  lower acyloxy,  $\text{C}_1\text{-C}_6$  lower acylamino with N substituted with  $\text{R}^6$ ,  $\text{CH}_2\text{OR}^5$ ,  $\text{CH}_2\text{NR}^6\text{R}^{6a}$ ,  $\text{R}_f$ ,  $\text{R}_f\text{O}$ , OH,  $\text{NH}_2$ , CN,  $\text{NO}_2$ , F, Cl, Br, I, or  $\text{N}_3$ ;

E is a bond,  $\text{S(O)}_m$ ,  $\text{NR}^6$ ,  $\text{C=O}$ ,  $\text{CO}_2$ ,  $\text{CONR}^6$ , O,  $-\text{OC=O}$ ,  $\text{NR}^6\text{C=O}$ ,  $\text{NR}^6\text{CO}_2$ ,  $\text{OC=ONR}^6$ ,  $\text{OCO}_2$ , or  $\text{NR}^6\text{CONR}^{6a}$ ;

20 F is  $(\text{CH}_2)_n$ ,  $(\text{CH}_2)_o\text{O}(\text{CH}_2)_p$ ,  $(\text{CH}_2)_o\text{NR}^6(\text{CH}_2)_p$ ,  $(\text{CH}_2)_o\text{NR}^6\text{CO}(\text{CH}_2)_p$ ,  $(\text{CH}_2)_o\text{CONR}^6(\text{CH}_2)_p$ ,  $(\text{CH}_2)_o(\text{CR}^6=\text{CR}^6)_q(\text{CH}_2)_p$ ,  $(\text{CH}_2)_o-(\text{C}\equiv\text{C})_q-(\text{CH}_2)_p$ ;

G is a bond, O,  $\text{NR}^6$ , CO,  $\text{CO}_2$ , OCO,  $\text{OCO}_2$ ,  $\text{S(O)}_m$ ,  $\text{CONR}^6$ ,  $\text{NR}^6\text{CO}$ ,  $\text{NR}^6\text{CO}_2$ ,  $\text{OCONR}^6$ ,  $\text{NR}^6\text{CONR}^{6a}$ , or G can optionally be attached to  $\text{Ar}^2$  at two contiguous C atoms to form a 5- to 7-membered partially saturated ring, which contains 0, 1, 25 or 2 heteroatoms selected from the group consisting of O, N, and S;

X, X<sup>1</sup> are independently O or S

Z<sup>2</sup> is nothing, H or Ar<sup>1</sup> optionally substituted with Y<sup>1</sup> and Y<sup>2</sup>;

R<sup>1</sup>, R<sup>2</sup>, R<sup>3</sup>, and R<sup>4</sup>, are each independently selected from H, C<sub>1</sub>-C<sub>6</sub> lower alkyl, C<sub>3</sub>-C<sub>6</sub> lower alkenyl, C<sub>3</sub>-C<sub>6</sub> lower alkynyl, C<sub>3</sub>-C<sub>6</sub> lower cycloalkyl, C<sub>4</sub>-C<sub>6</sub> lower cycloalkenyl, or independently R<sup>1</sup> and R<sup>2</sup> or R<sup>3</sup> and R<sup>4</sup> can be taken together to form a 5 to 8-membered ring containing 2-7 carbon atoms, the 5 to 8-membered ring optionally substituted with zero to 3 substituents selected from the group C<sub>1</sub>-C<sub>4</sub> lower alkyl, C<sub>1</sub>-C<sub>4</sub> lower alkoxy, C<sub>1</sub>-C<sub>4</sub> lower alkylamino, C<sub>1</sub>-C<sub>4</sub> lower dialkylamino, amino, hydroxyl, hydroxymethyl, methoxymethyl, phenyl, substituted phenyl, benzyl, substituted benzyl;

U and V are each independently a bond, O or NR<sup>6</sup>;

R<sup>5</sup> R<sup>6</sup> and R<sup>6a</sup> are each independently C<sub>1</sub>-C<sub>6</sub> alkyl, C<sub>3</sub>-C<sub>6</sub> cycloalkyl, C<sub>3</sub>-C<sub>6</sub> alkenyl, C<sub>3</sub>-C<sub>6</sub> cycloalkenyl, C<sub>3</sub>-C<sub>6</sub> alkynyl, and H;

R<sup>7</sup> and R<sup>8</sup> are each independently H, C<sub>1</sub>-C<sub>4</sub> lower alkyl, or are taken together to form a saturated C<sub>3</sub>-C<sub>6</sub> carbocyclic ring;

R<sub>F</sub> is C<sub>1</sub>-C<sub>4</sub> straight or branched lower perfluoroalkyl;

all lower alkyl, alkenyl and alkynyl groups including those linked via heteroatoms can be straight chain or branched;

m is 0, 1, or 2;

n is 0, 1, 2, 3, 4, 5, or 6;

o is 0, 1, 2, 3, 4, 5, or 6;

p is 0, 1, 2, 3, 4, 5, or 6; and

q is 0, 1, 2, 3, 4, 5, or 6;

with the provisos that

when A is a bond or O, B is  $P(O)(OR^3)(OR^4)$ , and D is selected from the group H, OH,  $OCOCH_3$ , and  $NH_2$ , and when  $R^1 = R^2$  and  $R^3 = R^4$ , and both are selected from the group H or unsubstituted  $C_1$ - $C_4$  lower alkyl, and E and G are bonds, and F is  $(CH_2)_n$  where n is 0, and both  $Ar^1$  and  $Ar^2$  are phenyl, then at least one of  $Y^1$ ,  $Y^2$ ,  $Z^1$ , or  $Z^2$  must not be H; and

when A is a bond or  $CH_2$ , and B is  $P(O)(OR^3)(OR^4)$ , and either D is H or  $C_1$ - $C_4$  lower alkyl where L is  $CH_2$ , or D is absent, with  $L \equiv C$  taken together represent an ethenylidene group, and  $Ar^1$  is phenyl, and E is a bond or O, and  $R^1 = R^2$  and  $R^3 = R^4$ , and both are drawn from the group H or  $C_1$ - $C_6$  unsubstituted lower alkyl, then one of  $Y^1$  and  $Y^2$  must be other than H or unsubstituted  $C_1$ - $C_4$  lower alkyl or unsubstituted  $C_1$ - $C_4$  lower alkoxy; and

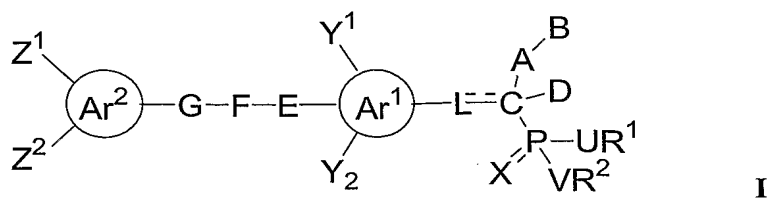
when A is O, and B is H or  $P(O)(OR^3)(OR^4)$ , and  $R^1$ ,  $R^2$ ,  $R^3$ , and  $R^4$  are all selected from the group H or  $C_1$ - $C_6$  unsubstituted lower alkyl, and D is H, and L is a bond, and  $Ar^1$  is phenyl, and E is other than a bond or O, then one of  $Y^1$  or  $Y^2$  must be other than H, or  $C_1$ - $C_4$  unsubstituted lower alkyl or  $C_1$ - $C_4$  unsubstituted lower alkoxy;

or a pharmaceutically acceptable salt thereof; and

a therapeutically effective amount of a compound known to be effective for regulating HDL or LDL levels.

20

29. A method of treating disease states related to HDL or LDL cholesterol levels comprising administering to a mammal in need of such treatment a therapeutically effective amount of a pharmaceutical formulation comprising a compound of the formula (I):



wherein

A is a bond, O, CH<sub>2</sub>, CHF, CF<sub>2</sub>, or NR<sub>6</sub>;

B is H, C<sub>1</sub>-C<sub>6</sub> lower alkyl, or P(=X<sup>1</sup>)(UR<sup>3</sup>)(VR<sup>4</sup>);

5 D is a) H or lower alkyl, wherein the L=C bond is a single bond; or

b) OH, OCOR<sup>5</sup>, NH<sub>2</sub>, NR<sup>6</sup>R<sup>6a</sup>, or NHCOR<sup>5</sup>, wherein the L=C bond is a single bond, with the proviso that A is CH<sub>2</sub>, CHF, CF<sub>2</sub>;

L is a) NR<sup>6</sup>, CR<sup>7</sup>R<sup>8</sup>, -OCR<sup>7</sup>R<sup>8</sup>-, -NR<sup>6</sup>CR<sup>7</sup>R<sup>8</sup>-, or -S(O)<sub>m</sub>CR<sup>7</sup>R<sup>8</sup>-, wherein the L=C bond is a single bond; or

10 b) CR<sup>7</sup>, wherein the L=C bond is a double bond, with the proviso that D is absent when the L=C bond is a double bond; or

c) absent, wherein C is covalently bonded by a single bond to Ar<sup>1</sup>;

Ar<sup>1</sup> and Ar<sup>2</sup> are each independently mono- or bicyclic aromatic rings of 5-12 atoms,

including, but not limited to phenyl, pyridyl, pyrimidyl, pyrazinyl, pyridazinyl,

15 thienyl, furanyl, pyrrolyl, imidazyl, pyrazolyl, oxazolyl, isoxazolyl, thiazolyl,

isothiazolyl, 1,3,4-oxadiazolyl, 1,2,4-oxadiazolyl, 1,3,4-thiadiazolyl, 1,2,3-

triazolyl, 1,3,4-triazolyl, 1,2,4-triazinyl, 1,3,5-triazinyl, benzofuranyl,

benzothienyl, indolyl, indazolyl, benzimidazyl, benzoxazolyl, benzoisoxazolyl,

benzothiazolyl, benzoisothiazolyl, quinolinyl, isoquinolinyl, quinazolinyl,

20 quinoxalinyl, naphthyridyl, or purinyl;

Y<sup>1</sup>, Y<sup>2</sup>, and Z<sup>1</sup> are each independently a lone electron pair, H, C<sub>1</sub>-C<sub>6</sub> lower alkyl, C<sub>2</sub>-C<sub>6</sub> lower alkenyl, C<sub>2</sub>-C<sub>6</sub> lower alkynyl, C<sub>1</sub>-C<sub>6</sub> lower alkoxy, C<sub>1</sub>-C<sub>6</sub> lower

alkylamino, C<sub>1</sub>-C<sub>6</sub> lower dialkylamino, C<sub>2</sub>-C<sub>6</sub> lower cycloalkyl, C<sub>4</sub>-C<sub>6</sub> lower cycloalkenyl, C<sub>1</sub>-C<sub>6</sub> lower thioalkyl, C<sub>1</sub>-C<sub>6</sub> lower sulfinylalkyl, C<sub>1</sub>-C<sub>6</sub> lower sulfonylalkyl, C<sub>1</sub>-C<sub>6</sub> lower acyloxy, C<sub>1</sub>-C<sub>6</sub> lower acylamino with N substituted with R<sup>6</sup>, CH<sub>2</sub>OR<sup>5</sup>, CH<sub>2</sub>NR<sup>6</sup>R<sup>6a</sup>, R<sub>f</sub>, R<sub>f</sub>O, OH, NH<sub>2</sub>, CN, NO<sub>2</sub>, F, Cl, Br, I, or N<sub>3</sub>;

5 E is a bond, S(O)<sub>m</sub>, NR<sup>6</sup>, C=O, CO<sub>2</sub>, CONR<sup>6</sup>, O, -OC=O, NR<sup>6</sup>C=O, NR<sup>6</sup>CO<sub>2</sub>, OC=ONR<sup>6</sup>, OCO<sub>2</sub>, or NR<sup>6</sup>CONR<sup>6a</sup>;

F is (CH<sub>2</sub>)<sub>n</sub>, (CH<sub>2</sub>)<sub>o</sub>O(CH<sub>2</sub>)<sub>p</sub>, (CH<sub>2</sub>)<sub>o</sub>NR<sup>6</sup>(CH<sub>2</sub>)<sub>p</sub>, (CH<sub>2</sub>)<sub>o</sub>NR<sup>6</sup>CO(CH<sub>2</sub>)<sub>p</sub>, (CH<sub>2</sub>)<sub>o</sub>CONR<sup>6</sup>(CH<sub>2</sub>)<sub>p</sub>, (CH<sub>2</sub>)<sub>o</sub>(CR<sup>6</sup>=CR<sup>6</sup>)<sub>q</sub>(CH<sub>2</sub>)<sub>p</sub>, (CH<sub>2</sub>)<sub>o</sub>-(C≡C)<sub>q</sub>-(CH<sub>2</sub>)<sub>p</sub>;

G is a bond, O, NR<sup>6</sup>, CO, CO<sub>2</sub>, OCO, OCO<sub>2</sub>, S(O)<sub>m</sub>, CONR<sup>6</sup>, NR<sup>6</sup>CO, NR<sup>6</sup>CO<sub>2</sub>,  
10 OCONR<sup>6</sup>, NR<sup>6</sup>CONR<sup>6a</sup>, or G can optionally be attached to Ar<sup>2</sup> at two contiguous C atoms to form a 5- to 7-membered partially saturated ring, which contains 0, 1, or 2 heteroatoms selected from the group consisting of O, N, and S;

X, X<sup>1</sup> are independently O or S

Z<sup>2</sup> is nothing, H or Ar<sup>1</sup> optionally substituted with Y<sup>1</sup> and Y<sup>2</sup>;

15 R<sup>1</sup>, R<sup>2</sup>, R<sup>3</sup>, and R<sup>4</sup>, are each independently selected from H, C<sub>1</sub>-C<sub>6</sub> lower alkyl, C<sub>3</sub>-C<sub>6</sub> lower alkenyl, C<sub>3</sub>-C<sub>6</sub> lower alkynyl, C<sub>3</sub>-C<sub>6</sub> lower cycloalkyl, C<sub>4</sub>-C<sub>6</sub> lower cycloalkenyl, or independently R<sup>1</sup> and R<sup>2</sup> or R<sup>3</sup> and R<sup>4</sup> can be taken together to form a 5 to 8-membered ring containing 2-7 carbon atoms, the 5 to 8-membered ring optionally substituted with zero to 3 substituents selected from the group C<sub>1</sub>-  
20 C<sub>4</sub> lower alkyl, C<sub>1</sub>-C<sub>4</sub> lower alkoxy, C<sub>1</sub>-C<sub>4</sub> lower alkylamino, C<sub>1</sub>-C<sub>4</sub> lower dialkylamino, amino, hydroxyl, hydroxymethyl, methoxymethyl, phenyl, substituted phenyl, benzyl, substituted benzyl;

U and V are each independently a bond, O or NR<sup>6</sup>;

R<sup>5</sup> R<sup>6</sup> and R<sup>6a</sup> are each independently C<sub>1</sub>-C<sub>6</sub> alkyl, C<sub>3</sub>-C<sub>6</sub> cycloalkyl, C<sub>3</sub>-C<sub>6</sub> alkenyl,  
25 C<sub>3</sub>-C<sub>6</sub> cycloalkenyl, C<sub>3</sub>-C<sub>6</sub> alkynyl, and H;

$R^7$  and  $R^8$  are each independently H,  $C_1$ - $C_4$  lower alkyl, or are taken together to form a saturated  $C_3$ - $C_6$  carbocyclic ring;

$R_f$  is  $C_1$ - $C_4$  straight or branched lower perfluoroalkyl;

all lower alkyl, alkenyl and alkynyl groups including those linked via heteroatoms can  
5 be straight chain or branched;

m is 0, 1, or 2;

n is 0, 1, 2, 3, 4, 5, or 6;

o is 0, 1, 2, 3, 4, 5, or 6;

p is 0, 1, 2, 3, 4, 5, or 6; and

10 q is 0, 1, 2, 3, 4, 5, or 6;

with the provisos that

when A is a bond or O, B is  $P(O)(OR^3)(OR^4)$ , and D is selected from the group H, OH,  $OCOCH_3$ , and  $NH_2$ , and when  $R^1 = R^2$  and  $R^3 = R^4$ , and both are selected from the group H or unsubstituted  $C_1$ - $C_4$  lower alkyl, and E and G are bonds, and F is  
15  $(CH_2)_n$  where n is 0, and both  $Ar^1$  and  $Ar^2$  are phenyl, then at least one of  $Y^1$ ,  $Y^2$ ,  $Z^1$ , or  $Z^2$  must not be H; and

when A is a bond or  $CH_2$ , and B is  $P(O)(OR^3)(OR^4)$ , and either D is H or  $C_1$ - $C_4$  lower alkyl where L is  $CH_2$ , or D is absent, with  $L \equiv C$  taken together represent an ethenylidene group, and  $Ar^1$  is phenyl, and E is a bond or O, and  $R^1 = R^2$  and  $R^3 = R^4$ ,  
20 and both are drawn from the group H or  $C_1$ - $C_6$  unsubstituted lower alkyl, then one of  $Y^1$  and  $Y^2$  must be other than H or unsubstituted  $C_1$ - $C_4$  lower alkyl or unsubstituted  $C_1$ - $C_4$  lower alkoxy; and

when A is O, and B is H or  $P(O)(OR^3)(OR^4)$ , and  $R^1$ ,  $R^2$ ,  $R^3$ , and  $R^4$  are all selected from the group H or  $C_1$ - $C_6$  unsubstituted lower alkyl, and D is H, and L is a  
25 bond, and  $Ar^1$  is phenyl, and E is other than a bond or O, then one of  $Y^1$  or  $Y^2$  must

- be other than H, or C<sub>1</sub>-C<sub>4</sub> unsubstituted lower alkyl or C<sub>1</sub>-C<sub>4</sub> unsubstituted lower alkoxy;
- or pharmaceutically acceptable salt thereof;
- a pharmaceutically acceptable carrier, excipient, solvent, adjuvant or diluent;
- 5 and optionally, a therapeutically effective amount of a compound known to be effective for regulating HDL or LDL levels.

30. The method according to any of Claims 27-29, wherein the mammal is a human.

10

31. The method according to any of Claims 27-29, wherein the effective amount is administered in a dosage of between about 0.1 mg to about 5000 mg per day.

32. The method according to any of Claims 27-29, wherein the effective  
15 amount comprises a dosage of between about 50 mg to about 500 mg per day.

33. The method according to any of Claims 27-29, wherein the effective amount of the pharmaceutical formulation is administered orally.

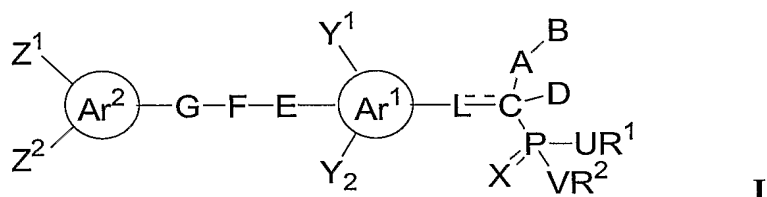
20 34. The method according to any of Claims 27-29, wherein the effective amount of the pharmaceutical formulation is administered depot injection.

35. The method according to Claim 28, wherein the compound known to be effective for regulating HDL or LDL levels is selected from the group consisting of  
25 statins, fibrates, bile acid sequestrants, and cholesterol uptake inhibitors.



36. The method according to Claim 35, wherein the compound known to be effective for regulating HDL or LDL levels is selected from lovastatin, simvastatin, pravastatin, atorvastatin, cerivastatin, niacin, clofibrate, bezafibrate, gemfibrozil, cholestyramine, phytosteroids, and ezetimibe

37. A method of lowering blood triglyceride levels comprising administering to a mammal in need of such treatment a therapeutically effective amount of a pharmaceutical formulation comprising a compound of the formula (I):



wherein

A is a bond, O, CH<sub>2</sub>, CHF, CF<sub>2</sub>, or NR<sub>6</sub>;

B is H, C<sub>1</sub>-C<sub>6</sub> lower alkyl, or P(=X<sup>1</sup>)(UR<sup>3</sup>)(VR<sup>4</sup>);

D is a) H or lower alkyl, wherein the L=C bond is a single bond; or

b) OH, OCOR<sup>5</sup>, NH<sub>2</sub>, NR<sup>6</sup>R<sup>6a</sup>, or NHCOR<sup>5</sup>, wherein the L=C bond is a single bond, with the proviso that A is CH<sub>2</sub>, CHF, CF<sub>2</sub>;

L is a) NR<sup>6</sup>, CR<sup>7</sup>R<sup>8</sup>, -OCR<sup>7</sup>R<sup>8</sup>-, -NR<sup>6</sup>CR<sup>7</sup>R<sup>8</sup>-, or -S(O)<sub>m</sub>CR<sup>7</sup>R<sup>8</sup>-, wherein the L=C bond is a single bond; or

b) CR<sup>7</sup>, wherein the L=C bond is a double bond, with the proviso that D is absent when the L=C bond is a double bond; or

c) absent, wherein C is covalently bonded by a single bond to Ar<sup>1</sup>;

Ar<sup>1</sup> and Ar<sup>2</sup> are each independently mono- or bicyclic aromatic rings of 5-12 atoms, including, but not limited to phenyl, pyridyl, pyrimidyl, pyrazinyl, pyridazinyl, thienyl, furanyl, pyrrolyl, imidazolyl, pyrazolyl, oxazolyl, isoxazolyl, thiazolyl, isothiazolyl, 1,3,4-oxadiazolyl, 1,2,4-oxadiazolyl, 1,3,4-thiadiazolyl, 1,2,3-  
 5 triazolyl, 1,3,4-triazolyl, 1,2,4-triazinyl, 1,3,5-triazinyl, benzofuranyl, benzothienyl, indolyl, indazolyl, benzimidazolyl, benzoxazolyl, benzoisoxazolyl, benzothiazolyl, benzoisothiazolyl, quinolinyl, isoquinolinyl, quinazolinyl, quinoxalinyl, naphthyridyl, or purinyl;

Y<sup>1</sup>, Y<sup>2</sup>, and Z<sup>1</sup> are each independently a lone electron pair, H, C<sub>1</sub>-C<sub>6</sub> lower alkyl, C<sub>2</sub>-  
 10 C<sub>6</sub> lower alkenyl, C<sub>2</sub>-C<sub>6</sub> lower alkynyl, C<sub>1</sub>-C<sub>6</sub> lower alkoxy, C<sub>1</sub>-C<sub>6</sub> lower alkylamino, C<sub>1</sub>-C<sub>6</sub> lower dialkylamino, C<sub>2</sub>-C<sub>6</sub> lower cycloalkyl, C<sub>4</sub>-C<sub>6</sub> lower cycloalkenyl, C<sub>1</sub>-C<sub>6</sub> lower thioalkyl, C<sub>1</sub>-C<sub>6</sub> lower sulfinylalkyl, C<sub>1</sub>-C<sub>6</sub> lower sulfonylalkyl, C<sub>1</sub>-C<sub>6</sub> lower acyloxy, C<sub>1</sub>-C<sub>6</sub> lower acylamino with N substituted with R<sup>6</sup>, CH<sub>2</sub>OR<sup>5</sup>, CH<sub>2</sub>NR<sup>6</sup>R<sup>6a</sup>, R<sub>f</sub>, R<sub>f</sub>O, OH, NH<sub>2</sub>, CN, NO<sub>2</sub>, F, Cl, Br, I, or N<sub>3</sub>;

15 E is a bond, S(O)<sub>m</sub>, NR<sup>6</sup>, C=O, CO<sub>2</sub>, CONR<sup>6</sup>, O, -OC=O, NR<sup>6</sup>C=O, NR<sup>6</sup>CO<sub>2</sub>, OC=ONR<sup>6</sup>, OCO<sub>2</sub>, or NR<sup>6</sup>CONR<sup>6a</sup>;

F is (CH<sub>2</sub>)<sub>n</sub>, (CH<sub>2</sub>)<sub>o</sub>O(CH<sub>2</sub>)<sub>p</sub>, (CH<sub>2</sub>)<sub>o</sub>NR<sup>6</sup>(CH<sub>2</sub>)<sub>p</sub>, (CH<sub>2</sub>)<sub>o</sub>NR<sup>6</sup>CO(CH<sub>2</sub>)<sub>p</sub>, (CH<sub>2</sub>)<sub>o</sub>CONR<sup>6</sup>(CH<sub>2</sub>)<sub>p</sub>, (CH<sub>2</sub>)<sub>o</sub>(CR<sup>6</sup>=CR<sup>6</sup>)<sub>q</sub>(CH<sub>2</sub>)<sub>p</sub>, (CH<sub>2</sub>)<sub>o</sub>-(C≡C)<sub>q</sub>-(CH<sub>2</sub>)<sub>p</sub>;

G is a bond, O, NR<sup>6</sup>, CO, CO<sub>2</sub>, OCO, OCO<sub>2</sub>, S(O)<sub>m</sub>, CONR<sup>6</sup>, NR<sup>6</sup>CO, NR<sup>6</sup>CO<sub>2</sub>,  
 20 OCONR<sup>6</sup>, NR<sup>6</sup>CONR<sup>6a</sup>, or G can optionally be attached to Ar<sup>2</sup> at two contiguous C atoms to form a 5- to 7-membered partially saturated ring, which contains 0, 1, or 2 heteroatoms selected from the group consisting of O, N, and S;

X, X<sup>1</sup> are independently O or S

Z<sup>2</sup> is nothing, H or Ar<sup>1</sup> optionally substituted with Y<sup>1</sup> and Y<sup>2</sup>;

$R^1$ ,  $R^2$ ,  $R^3$ , and  $R^4$ , are each independently selected from H, C<sub>1</sub>-C<sub>6</sub> lower alkyl, C<sub>3</sub>-C<sub>6</sub> lower alkenyl, C<sub>3</sub>-C<sub>6</sub> lower alkynyl, C<sub>3</sub>-C<sub>6</sub> lower cycloalkyl, C<sub>4</sub>-C<sub>6</sub> lower cycloalkenyl, or independently  $R^1$  and  $R^2$  or  $R^3$  and  $R^4$  can be taken together to form a 5 to 8-membered ring containing 2-7 carbon atoms, the 5 to 8-membered ring optionally substituted with zero to 3 substituents selected from the group C<sub>1</sub>-C<sub>4</sub> lower alkyl, C<sub>1</sub>-C<sub>4</sub> lower alkoxy, C<sub>1</sub>-C<sub>4</sub> lower alkylamino, C<sub>1</sub>-C<sub>4</sub> lower dialkylamino, amino, hydroxyl, hydroxymethyl, methoxymethyl, phenyl, substituted phenyl, benzyl, substituted benzyl;

U and V are each independently a bond, O or NR<sup>6</sup>;

$R^5$ ,  $R^6$  and  $R^{6a}$  are each independently C<sub>1</sub>-C<sub>6</sub> alkyl, C<sub>3</sub>-C<sub>6</sub> cycloalkyl, C<sub>3</sub>-C<sub>6</sub> alkenyl, C<sub>3</sub>-C<sub>6</sub> cycloalkenyl, C<sub>3</sub>-C<sub>6</sub> alkynyl, and H;

$R^7$  and  $R^8$  are each independently H, C<sub>1</sub>-C<sub>4</sub> lower alkyl, or are taken together to form a saturated C<sub>3</sub>-C<sub>6</sub> carbocyclic ring;

$R_f$  is C<sub>1</sub>-C<sub>4</sub> straight or branched lower perfluoroalkyl;

all lower alkyl, alkenyl and alkynyl groups including those linked via heteroatoms can be straight chain or branched;

m is 0, 1, or 2;

n is 0, 1, 2, 3, 4, 5, or 6;

o is 0, 1, 2, 3, 4, 5, or 6;

p is 0, 1, 2, 3, 4, 5, or 6; and

q is 0, 1, 2, 3, 4, 5, or 6;

with the provisos that

when A is a bond or O, B is P(O)(OR<sup>3</sup>)(OR<sup>4</sup>), and D is selected from the group H, OH, OCOCH<sub>3</sub>, and NH<sub>2</sub>, and when  $R^1 = R^2$  and  $R^3 = R^4$ , and both are selected from the group H or unsubstituted C<sub>1</sub>-C<sub>4</sub> lower alkyl, and E and G are bonds, and F is

(CH<sub>2</sub>)<sub>n</sub> where n is 0, and both Ar<sup>1</sup> and Ar<sup>2</sup> are phenyl, then at least one of Y<sup>1</sup>, Y<sup>2</sup>, Z<sup>1</sup>, or Z<sup>2</sup> must not be H; and

when A is a bond or CH<sub>2</sub>, and B is P(O)(OR<sup>3</sup>)(OR<sup>4</sup>), and either D is H or C<sub>1</sub>-C<sub>4</sub> lower alkyl where L is CH<sub>2</sub>, or D is absent, with L≡C taken together represent an ethenylidene group, and Ar<sup>1</sup> is phenyl, and E is a bond or O, and R<sup>1</sup> = R<sup>2</sup> and R<sup>3</sup> = R<sup>4</sup>, and both are drawn from the group H or C<sub>1</sub>-C<sub>6</sub> unsubstituted lower alkyl, then one of Y<sup>1</sup> and Y<sup>2</sup> must be other than H or unsubstituted C<sub>1</sub>-C<sub>4</sub> lower alkyl or unsubstituted C<sub>1</sub>-C<sub>4</sub> lower alkoxy; and

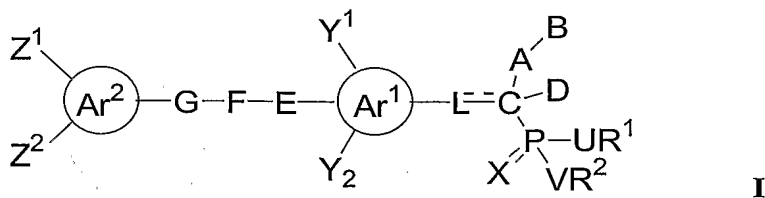
when A is O, and B is H or P(O)(OR<sup>3</sup>)(OR<sup>4</sup>), and R<sup>1</sup>, R<sup>2</sup>, R<sup>3</sup>, and R<sup>4</sup> are all selected from the group H or C<sub>1</sub>-C<sub>6</sub> unsubstituted lower alkyl, and D is H, and L is a bond, and Ar<sup>1</sup> is phenyl, and E is other than a bond or O, then one of Y<sup>1</sup> or Y<sup>2</sup> must be other than H, or C<sub>1</sub>-C<sub>4</sub> unsubstituted lower alkyl or C<sub>1</sub>-C<sub>4</sub> unsubstituted lower alkoxy;

or pharmaceutically acceptable salt thereof;

a pharmaceutically acceptable carrier, excipient, solvent, adjuvant or diluent; and optionally, a therapeutically effective amount of a compound known to be effective for regulating triglyceride levels.

38. The method of Claim 37, wherein the compound known to be effective for regulating triglyceride levels comprises a fibrate.

39. A method of lowering blood glucose levels comprising administering to a mammal in need of such treatment a therapeutically effective amount of a pharmaceutical formulation comprising a compound of the formula (I):



wherein

A is a bond, O, CH<sub>2</sub>, CHF, CF<sub>2</sub>, or NR<sub>6</sub>;

B is H, C<sub>1</sub>-C<sub>6</sub> lower alkyl, or P(=X<sup>1</sup>)(UR<sup>3</sup>)(VR<sup>4</sup>);

5 D is a) H or lower alkyl, wherein the L=C bond is a single bond; or

b) OH, OCOR<sup>5</sup>, NH<sub>2</sub>, NR<sup>6</sup>R<sup>6a</sup>, or NHCOR<sup>5</sup>, wherein the L=C bond is a single bond, with the proviso that A is CH<sub>2</sub>, CHF, CF<sub>2</sub>;

L is a) NR<sup>6</sup>, CR<sup>7</sup>R<sup>8</sup>, -OCR<sup>7</sup>R<sup>8</sup>-, -NR<sup>6</sup>CR<sup>7</sup>R<sup>8</sup>-, or -S(O)<sub>m</sub>CR<sup>7</sup>R<sup>8</sup>-, wherein the L=C bond is a single bond; or

10 b) CR<sup>7</sup>, wherein the L=C bond is a double bond, with the proviso that D is absent when the L=C bond is a double bond; or

c) absent, wherein C is covalently bonded by a single bond to Ar<sup>1</sup>;

Ar<sup>1</sup> and Ar<sup>2</sup> are each independently mono- or bicyclic aromatic rings of 5-12 atoms, including, but not limited to phenyl, pyridyl, pyrimidyl, pyrazinyl, pyridazinyl, thienyl, furanyl, pyrrolyl, imidazyl, pyrazolyl, oxazolyl, isoxazolyl, thiazolyl, isothiazolyl, 1,3,4-oxadiazolyl, 1,2,4-oxadiazolyl, 1,3,4-thiadiazolyl, 1,2,3-triazolyl, 1,3,4-triazolyl, 1,2,4-triazinyl, 1,3,5-triazinyl, benzofuranyl, benzothienyl, indolyl, indazolyl, benzimidazyl, benzoxazolyl, benzoisoxazolyl, benzothiazolyl, benzoisothiazolyl, quinolinyl, isoquinolinyl, quinazolinyl, quinoxalinyl, naphthyridyl, or purinyl;

20 Y<sup>1</sup>, Y<sup>2</sup>, and Z<sup>1</sup> are each independently a lone electron pair, H, C<sub>1</sub>-C<sub>6</sub> lower alkyl, C<sub>2</sub>-C<sub>6</sub> lower alkenyl, C<sub>2</sub>-C<sub>6</sub> lower alkynyl, C<sub>1</sub>-C<sub>6</sub> lower alkoxy, C<sub>1</sub>-C<sub>6</sub> lower

alkylamino, C<sub>1</sub>-C<sub>6</sub> lower dialkylamino, C<sub>2</sub>-C<sub>6</sub> lower cycloalkyl, C<sub>4</sub>-C<sub>6</sub> lower cycloalkenyl, C<sub>1</sub>-C<sub>6</sub> lower thioalkyl, C<sub>1</sub>-C<sub>6</sub> lower sulfinylalkyl, C<sub>1</sub>-C<sub>6</sub> lower sulfonylalkyl, C<sub>1</sub>-C<sub>6</sub> lower acyloxy, C<sub>1</sub>-C<sub>6</sub> lower acylamino with N substituted with R<sup>6</sup>, CH<sub>2</sub>OR<sup>5</sup>, CH<sub>2</sub>NR<sup>6</sup>R<sup>6a</sup>, R<sub>f</sub>, R<sub>f</sub>O, OH, NH<sub>2</sub>, CN, NO<sub>2</sub>, F, Cl, Br, I, or N<sub>3</sub>;

5 E is a bond, S(O)<sub>m</sub>, NR<sup>6</sup>, C=O, CO<sub>2</sub>, CONR<sup>6</sup>, O, -OC=O, NR<sup>6</sup>C=O, NR<sup>6</sup>CO<sub>2</sub>, OC=ONR<sup>6</sup>, OCO<sub>2</sub>, or NR<sup>6</sup>CONR<sup>6a</sup>;

F is (CH<sub>2</sub>)<sub>n</sub>, (CH<sub>2</sub>)<sub>o</sub>O(CH<sub>2</sub>)<sub>p</sub>, (CH<sub>2</sub>)<sub>o</sub>NR<sup>6</sup>(CH<sub>2</sub>)<sub>p</sub>, (CH<sub>2</sub>)<sub>o</sub>NR<sup>6</sup>CO(CH<sub>2</sub>)<sub>p</sub>, (CH<sub>2</sub>)<sub>o</sub>CONR<sup>6</sup>(CH<sub>2</sub>)<sub>p</sub>, (CH<sub>2</sub>)<sub>o</sub>(CR<sup>6</sup>=CR<sup>6</sup>)<sub>q</sub>(CH<sub>2</sub>)<sub>p</sub>, (CH<sub>2</sub>)<sub>o</sub>-(C≡C)<sub>q</sub>-(CH<sub>2</sub>)<sub>p</sub>;

G is a bond, O, NR<sup>6</sup>, CO, CO<sub>2</sub>, OCO, OCO<sub>2</sub>, S(O)<sub>m</sub>, CONR<sup>6</sup>, NR<sup>6</sup>CO, NR<sup>6</sup>CO<sub>2</sub>,  
 10 OCONR<sup>6</sup>, NR<sup>6</sup>CONR<sup>6a</sup>, or G can optionally be attached to Ar<sup>2</sup> at two contiguous C atoms to form a 5- to 7-membered partially saturated ring, which contains 0, 1, or 2 heteroatoms selected from the group consisting of O, N, and S;

X, X<sup>1</sup> are independently O or S

Z<sup>2</sup> is nothing, H or Ar<sup>1</sup> optionally substituted with Y<sup>1</sup> and Y<sup>2</sup>;

15 R<sup>1</sup>, R<sup>2</sup>, R<sup>3</sup>, and R<sup>4</sup>, are each independently selected from H, C<sub>1</sub>-C<sub>6</sub> lower alkyl, C<sub>3</sub>-C<sub>6</sub> lower alkenyl, C<sub>3</sub>-C<sub>6</sub> lower alkynyl, C<sub>3</sub>-C<sub>6</sub> lower cycloalkyl, C<sub>4</sub>-C<sub>6</sub> lower cycloalkenyl, or independently R<sup>1</sup> and R<sup>2</sup> or R<sup>3</sup> and R<sup>4</sup> can be taken together to form a 5 to 8-membered ring containing 2-7 carbon atoms, the 5 to 8-membered ring optionally substituted with zero to 3 substituents selected from the group C<sub>1</sub>-  
 20 C<sub>4</sub> lower alkyl, C<sub>1</sub>-C<sub>4</sub> lower alkoxy, C<sub>1</sub>-C<sub>4</sub> lower alkylamino, C<sub>1</sub>-C<sub>4</sub> lower dialkylamino, amino, hydroxyl, hydroxymethyl, methoxymethyl, phenyl, substituted phenyl, benzyl, substituted benzyl;

U and V are each independently a bond, O or NR<sup>6</sup>;

R<sup>5</sup> R<sup>6</sup> and R<sup>6a</sup> are each independently C<sub>1</sub>-C<sub>6</sub> alkyl, C<sub>3</sub>-C<sub>6</sub> cycloalkyl, C<sub>3</sub>-C<sub>6</sub> alkenyl,  
 25 C<sub>3</sub>-C<sub>6</sub> cycloalkenyl, C<sub>3</sub>-C<sub>6</sub> alkynyl, and H;

$R^7$  and  $R^8$  are each independently H,  $C_1$ - $C_4$  lower alkyl, or are taken together to form a saturated  $C_3$ - $C_6$  carbocyclic ring;

$R_f$  is  $C_1$ - $C_4$  straight or branched lower perfluoroalkyl;

all lower alkyl, alkenyl and alkynyl groups including those linked via heteroatoms can  
5 be straight chain or branched;

m is 0, 1, or 2;

n is 0, 1, 2, 3, 4, 5, or 6;

o is 0, 1, 2, 3, 4, 5, or 6;

p is 0, 1, 2, 3, 4, 5, or 6; and

10 q is 0, 1, 2, 3, 4, 5, or 6;

with the provisos that

when A is a bond or O, B is  $P(O)(OR^3)(OR^4)$ , and D is selected from the group H, OH,  $OCOCH_3$ , and  $NH_2$ , and when  $R^1 = R^2$  and  $R^3 = R^4$ , and both are selected from the group H or unsubstituted  $C_1$ - $C_4$  lower alkyl, and E and G are bonds, and F is  
15  $(CH_2)_n$  where n is 0, and both  $Ar^1$  and  $Ar^2$  are phenyl, then at least one of  $Y^1$ ,  $Y^2$ ,  $Z^1$ , or  $Z^2$  must not be H; and

when A is a bond or  $CH_2$ , and B is  $P(O)(OR^3)(OR^4)$ , and either D is H or  $C_1$ - $C_4$  lower alkyl where L is  $CH_2$ , or D is absent, with  $L=C$  taken together represent an ethenylidene group, and  $Ar^1$  is phenyl, and E is a bond or O, and  $R^1 = R^2$  and  $R^3 = R^4$ ,  
20 and both are drawn from the group H or  $C_1$ - $C_6$  unsubstituted lower alkyl, then one of  $Y^1$  and  $Y^2$  must be other than H or unsubstituted  $C_1$ - $C_4$  lower alkyl or unsubstituted  $C_1$ - $C_4$  lower alkoxy; and

when A is O, and B is H or  $P(O)(OR^3)(OR^4)$ , and  $R^1$ ,  $R^2$ ,  $R^3$ , and  $R^4$  are all selected from the group H or  $C_1$ - $C_6$  unsubstituted lower alkyl, and D is H, and L is a  
25 bond, and  $Ar^1$  is phenyl, and E is other than a bond or O, then one of  $Y^1$  or  $Y^2$  must

- be other than H, or C<sub>1</sub>-C<sub>4</sub> unsubstituted lower alkyl or C<sub>1</sub>-C<sub>4</sub> unsubstituted lower alkoxy;
- or pharmaceutically acceptable salt thereof;
- a pharmaceutically acceptable carrier, excipient, solvent, adjuvant or diluent;
- 5 and optionally, a therapeutically effective amount of a compound known to be effective for regulating glucose levels.

40. The method of Claim 39, wherein the compound known to be effective for regulating glucose levels is selected from rosiglitazone, pioglitazone, insulin, and  
10 metformin.



## INTERNATIONAL SEARCH REPORT

International Application No

PCT/US2004/029701

## A. CLASSIFICATION OF SUBJECT MATTER

IPC 7 C07F9/58 C07F9/6558 C07F9/572 C07F9/6571 C07F9/6584  
 C07F9/653 C07F9/6539 C07F9/40 C07F9/6561

According to International Patent Classification (IPC) or to both national classification and IPC

## B. FIELDS SEARCHED

Minimum documentation searched (classification system followed by classification symbols)

IPC 7 C07F

Documentation searched other than minimum documentation to the extent that such documents are included in the fields searched

Electronic data base consulted during the international search (name of data base and, where practical, search terms used)

EPO-Internal, BIOSIS, CHEM ABS Data

## C. DOCUMENTS CONSIDERED TO BE RELEVANT

Category *	Citation of document, with indication, where appropriate, of the relevant passages	Relevant to claim No.
X	FUKUYAMA Y ET AL: "Total syntheses of plagiochins A and D, macrocyclic bis(bibenzyls), by Pd(0) catalysed intramolecular Stille-Kelly reaction" HETEROCYCLES, vol. 54, no. 1, 2001, pages 259-274, XP002313201 ISSN: 0385-5414 compound 20	1
A	WO 03/070179 A (ILEX PRODUCTS INC) 28 August 2003 (2003-08-28) cited in the application the whole document ----- -/--	1-40

☒ Further documents are listed in the continuation of box C.☒ Patent family members are listed in annex.

\* Special categories of cited documents:

- \*A\* document defining the general state of the art which is not considered to be of particular relevance
- \*E\* earlier document but published on or after the international filing date
- \*L\* document which may throw doubts on priority claim(s) or which is cited to establish the publication date of another citation or other special reason (as specified)
- \*O\* document referring to an oral disclosure, use, exhibition or other means
- \*P\* document published prior to the international filing date but later than the priority date claimed

- \*T\* later document published after the international filing date or priority date and not in conflict with the application but cited to understand the principle or theory underlying the invention
- \*X\* document of particular relevance; the claimed invention cannot be considered novel or cannot be considered to involve an inventive step when the document is taken alone
- \*Y\* document of particular relevance; the claimed invention cannot be considered to involve an inventive step when the document is combined with one or more other such documents, such combination being obvious to a person skilled in the art.
- \*Z\* document member of the same patent family

Date of the actual completion of the international search

13 January 2005

Date of mailing of the international search report

31/01/2005

Name and mailing address of the ISA

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## INTERNATIONAL SEARCH REPORT

International Application No

PCT/US2004/029701

## C.(Continuation) DOCUMENTS CONSIDERED TO BE RELEVANT

Category *	Citation of document, with indication, where appropriate, of the relevant passages	Relevant to claim No.
A	WO 03/070169 A (ILEX PRODUCTS INC) 28 August 2003 (2003-08-28) cited in the application the whole document -----	1-40
A	WO 02/26752 A (ILEX ONCOLOGY RES S A) 4 April 2002 (2002-04-04) cited in the application the whole document -----	1-40
A	WO 97/36597 A (GLAXO GROUP LIMITED) 9 October 1997 (1997-10-09) cited in the application the whole document & US 6 028 109 A (WILLSON TIMOTHY MARK) 22 February 2000 (2000-02-22) -----	1-40

## INTERNATIONAL SEARCH REPORT

International application No.  
PCT/US2004/029701

### Box II Observations where certain claims were found unsearchable (Continuation of item 2 of first sheet)

This International Search Report has not been established in respect of certain claims under Article 17(2)(a) for the following reasons:

1. ☒ Claims Nos.: 1-5, 7-11, 13-40 (all partially)  
because they relate to subject matter not required to be searched by this Authority, namely:  
Although claims 14-40 are directed to methods of treatment of the human body, the search has been carried out and based on the alleged effects of the compounds.
2. ☒ Claims Nos.: 1-5, 7-11, 13-40  
because they relate to parts of the International Application that do not comply with the prescribed requirements to such an extent that no meaningful International Search can be carried out, specifically:  
see FURTHER INFORMATION sheet PCT/ISA/210
3. ☐ Claims Nos.:  
because they are dependent claims and are not drafted in accordance with the second and third sentences of Rule 6.4(a).

### Box III Observations where unity of invention is lacking (Continuation of item 3 of first sheet)

This International Searching Authority found multiple inventions in this international application, as follows:

1. ☐ As all required additional search fees were timely paid by the applicant, this International Search Report covers all searchable claims.
2. ☐ As all searchable claims could be searched without effort justifying an additional fee, this Authority did not invite payment of any additional fee.
3. ☐ As only some of the required additional search fees were timely paid by the applicant, this International Search Report covers only those claims for which fees were paid, specifically claims Nos.:
4. ☐ No required additional search fees were timely paid by the applicant. Consequently, this international Search Report is restricted to the invention first mentioned in the claims; it is covered by claims Nos.:

#### Remark on Protest

- ☐ The additional search fees were accompanied by the applicant's protest.
- ☐ No protest accompanied the payment of additional search fees.

## FURTHER INFORMATION CONTINUED FROM PCT/ISA/ 210

## Continuation of Box II.1

Although claims 14-40 are directed to methods of treatment of the human body, the search has been carried out and based on the alleged effects of the compounds.

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## Continuation of Box II.2

Claims Nos.: 1-5,7-11,13-40

Present claims 1-4 relate to an extremely large number of possible compounds. In fact, the claims contain so many options that a lack of clarity (and conciseness) within the meaning of Article 6 PCT arises to such an extent as to render a meaningful search of the claims impossible. Consequently, the search has been carried out for those parts of the application which do appear to be clear (and concise), namely the compounds of claim 6 and has been formulated in such a way that structurally closely related compounds were also encompassed in the search. Limiting the search to the subject-matter of what is to be considered clear claim 5 was not deemed possible as the claim encompasses so many different combinations of heterocycles and aromatics that searching for all possible permutations of compounds of claim 5 was unfeasible on economic grounds due to the fact that numerous structure queries would have to be formulated, structure queries which could not be encompassed by a more broad general formula. By restricting the search to the subject-matter of claim 6 what can be seen as the preferred compounds of the application have been searched.

The applicant's attention is drawn to the fact that claims relating to inventions in respect of which no international search report has been established need not be the subject of an international preliminary examination (Rule 66.1(e) PCT). The applicant is advised that the EPO policy when acting as an International Preliminary Examining Authority is normally not to carry out a preliminary examination on matter which has not been searched. This is the case irrespective of whether or not the claims are amended following receipt of the search report or during any Chapter II procedure. If the application proceeds into the regional phase before the EPO, the applicant is reminded that a search may be carried out during examination before the EPO (see EPO Guideline C-VI, 8.5), should the problems which led to the Article 17(2) declaration be overcome.

# INTERNATIONAL SEARCH REPORT

Information on patent family members

International Application No

PCT/US2004/029701

Patent document cited in search report		Publication date	Patent family member(s)	Publication date
WO 03070179	A	28-08-2003	EP 1485106 A2 WO 03070179 A2	15-12-2004 28-08-2003
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